STUDIES IN THE CARBAZOLE SERIES

by

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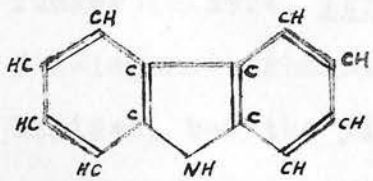
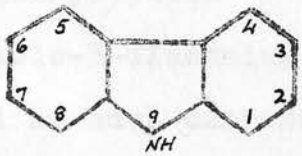
INTRODUCTION.

Carbazole was first discovered in 1872 as a constituent of coal tar by Graebe and Glaser (Ber.1872, 5, 12) and (Ann.1872, 163, 343). As a result of further investigations, Graebe advanced what later proved to be the correct constitution of the compound, and along with Ullmann introduced a useful synthesis of carbazole and its derivatives (Ann.1896, 291, 16).

In the literature, carbazole is found under such names as dibenzo-pyrrole and diphenylene-imine and the most usual nomenclature of the compound and its derivatives is shown by the following :



or simply,



(Ullmann, Ber.1898, 31, 1697).

Chemically, carbazole is an exceedingly stable compound. For example, it remains unchanged on distillation, and is unaffected by concentrated hydrochloric acid even at 300°C. (Graebe and Glaser, Ann.1872, 163,347). However, it forms substitution products, and also addition products with such reagents as picric acid and trinitrobenzene. These addition products are frequently used for identifying both the parent compound and its derivatives.

By reduction of carbazole with sodium and amyl alcohol, both dihydrocarbazole and tetrahydrocarbazole can be obtained (Schmidt and Schall, Ber. 1907, 40, 3229). Tetrahydrocarbazole on further reduction with tin and hydrochloric acid readily yields hexahydrocarbazole (Borsche, Witte and Bothe, Ann.1908, 359, 70.

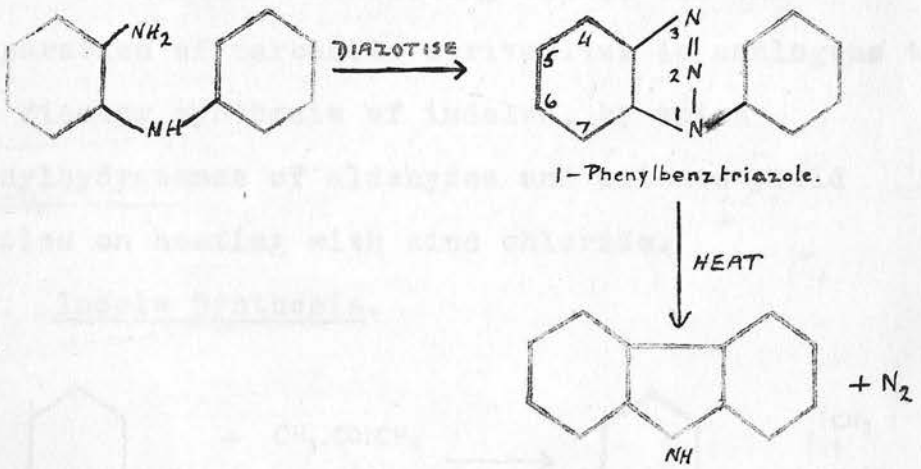
The Graebe-Ullmann method (see p. 3) was used successfully to prepare certain halogenated carbazoles (Ullmann, Ann.1904, 332, 97), and by the same method methylcarbazoles have also been obtained. Halogenated carbazoles can also be obtained directly from the parent compound, the 3- and then the 3:6-disubstituted derivatives being thus prepared. Tucker (J.1924, 125, 1146) has also prepared 3-halogeno-carbazoles from carbazole-3-diazonium halides, but the yields are small as much carbazole is also formed. Borsche, Witte and Bothe (Ann.1908, 359, 75) isolated methylcarbazoles by leading methyltetrahydrocarbazoles over lead oxide.

Certain of the carbazole acids have been prepared by the action of carbon dioxide on potassium carbazole at high temperatures under pressure, but more recently they have been obtained by oxidation of the tetrahydrocarbazole-carboxylic acids.

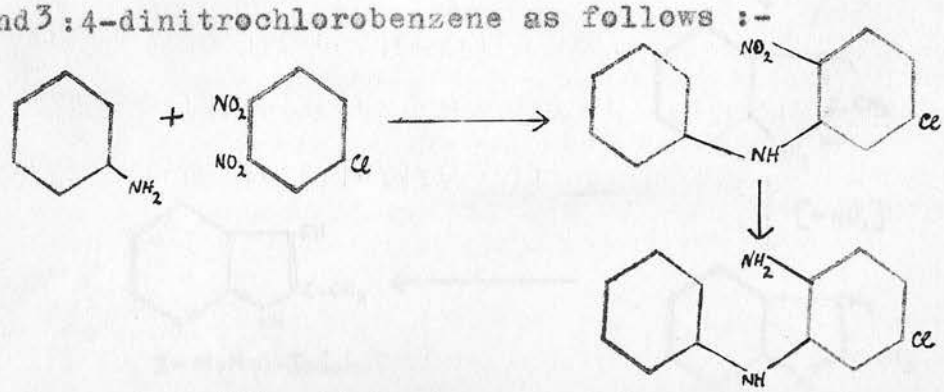
Direct nitration of carbazole under suitable conditions leads to mono-, di-, and tetra-nitrocarbazoles /

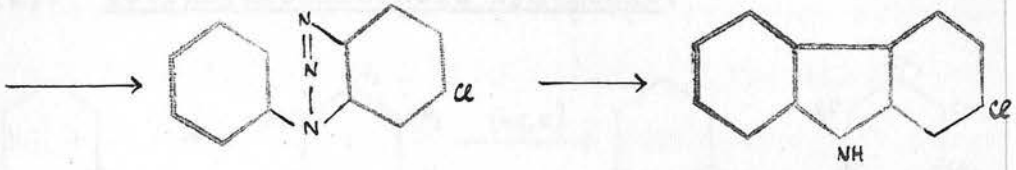
nitrocarbazoles, and this has been investigated mainly by Ziersch (Ber.1909, 42, 3797), Lindemann and Werther (Ber.1924, 57, 555,1316), Morgan and Mitchell (J.1931, 3283) and Tucker (J.1942, 500) . Lindemann has reduced the nitrocompounds to the corresponding aminocarbazoles.

The most widely applicable method so far has been that,already mentioned, of Graebe and Ullmann shown schematically as follows, starting with o-aminodiphenylamine :-



Moreover, the method has been employed, by the use of suitable substituted diphenylamines, to prepare a large number of substituted carbazoles; the method is also useful for orientation of the carbazoles. e.g. the preparation of 2-chlorocarbazole from aniline and 3:4-dinitrochlorobenzene as follows :-

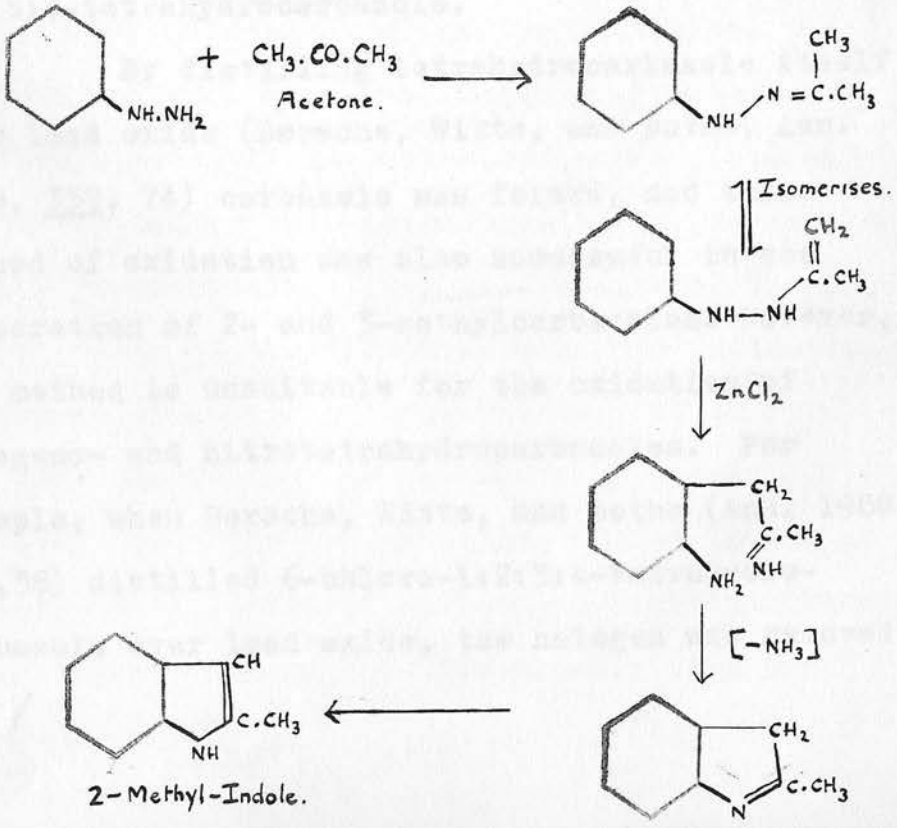




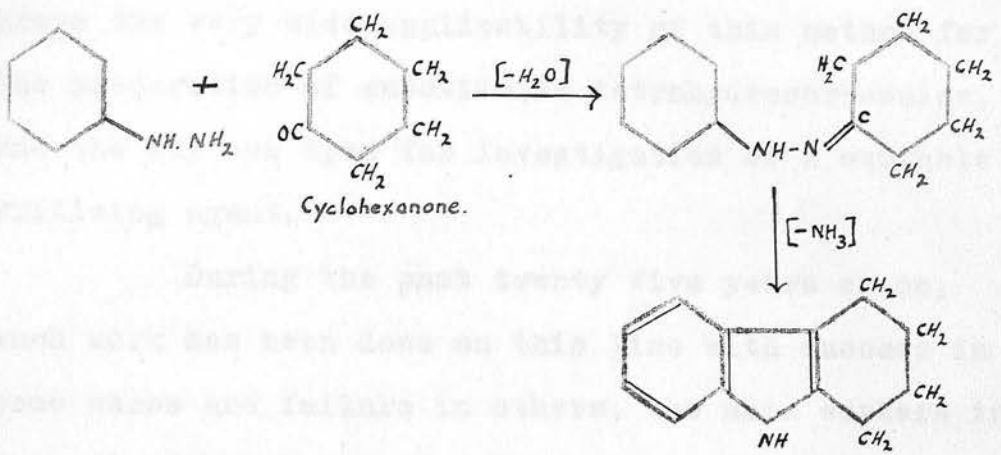
MacLean (Thesis, Edinburgh, 1941) , however, found that when 7-bromo-5-carboxy-1-phenyltriazole was distilled at 360°C with freshly-prepared quicklime (Ullmann,Ann.1904, 332, 82), both carbon dioxide and bromine were removed, and carbazole was obtained instead of 1-bromocarbazole as expected.

Another interesting method for the preparation of carbazole derivatives is analogous to the Fischer synthesis of indoles, by which phenylhydrazones of aldehydes and ketones yield indoles on heating with zinc chloride.

(1). Indole Synthesis.



(2). Tetrahydrocarbazole Synthesis.



Borsche, Witte, and Bothe (Ann.1908, 359, 60) have prepared by this method a very large number of substituted tetrahydrocarbazoles from substituted phenylhydrazines and substituted cyclohexanones. For example, 6-nitro-1:2:3:4-tetrahydrocarbazole can be obtained by condensing p-nitrophenylhydrazine with cyclohexanone, while condensation of m-methylcyclohexanone with phenylhydrazine yields 2-methyl-1:2:3:4-tetrahydrocarbazole.

By distilling tetrahydrocarbazole itself over lead oxide (Borsche, Witte, and Bothe, Ann. 1908, 359, 74) carbazole was formed, and this method of oxidation was also successful in the preparation of 2- and 3-methylcarbazoles. However, the method is unsuitable for the oxidation of halogeno- and nitrotetrahydrocarbazoles. For example, when Borsche, Witte, and Bothe (Ann. 1908, 359, 58) distilled 6-chloro-1:2:3:4-tetrahydrocarbazole over lead oxide, the halogen was removed and /

and carbazole resulted. However, they were able to prove the very wide applicability of this method for the preparation of substituted tetrahydrocarbazoles, and the way was open for investigation of a suitable oxidising agent.

During the past twenty five years or so, much work has been done on this line with success in some cases and failure in others, the main workers in this field being Perkin, Plant and co-workers, and Tucker and co-workers. Much of the work will be discussed in detail at a later stage in this thesis. For the present, mention will be made of some of the oxidising agents used and examples given of some of the results obtained.

Perkin and Plant (J.1921, 119, 1825) found that potassium permanganate did not oxidise tetrahydrocarbazole, but they noted the necessity for a suitable oxidising agent and suggested the use of mercuric acetate, by use of which they obtained a very small yield of carbazole and a 20% yield of 9-methylcarbazole by oxidation of the corresponding tetrahydro-compounds. They also mentioned the investigation of the effect of mercuric acetate on 6-nitro-1:2:3:4-tetrahydrocarbazole, but no results were ever reported. Later, the same authors (J.1923, 123, 676) used sulphur in boiling quinoline and so obtained small yields of carbazole, N-methylcarbazole, N-acetylcarbazole and 3-bromocarbazole from the

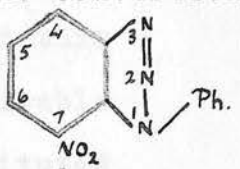
corresponding /

corresponding tetrahydrocarbazoles. 6-nitro-1:2:3:4-tetrahydrocarbazole however, on this treatment, yielded a black resin, and -COOEt was removed from 9-carbethoxytetrahydrocarbazole to give carbazole itself. In 1926, Oakeshott and Plant (J.1926, 1211) successfully obtained 3-methylcarbazole and 3:6-dimethylcarbazole by sulphur and quinoline dehydrogenations, but no yields are quoted.

Another reagent which has been used, not always with success, is palladised charcoal in an atmosphere of hydrogen. Moggridge and Plant used this reagent to oxidise the methyl esters of 6- and 8- carboxy-1:2:3:4-tetrahydrocarbazole, but when the tetrahydrocarboxylic acid itself was so treated, the -COOH was removed in the course of the oxidation and carbazole was obtained. These workers also found that oxidation of halogeno-tetrahydrocarbazoles by palladised charcoal resulted in removal of halogen simultaneously with oxidation, but they prepared 2-chlorocarbazole by oxidising 7-chloro-1:2:3:4-tetrahydrocarbazole with sulphur in quinoline.

Sufficient examples have been given to show that, although in some cases the specific reagent used has been successful in oxidising substituted tetrahydrocarbazoles to substituted carbazoles, no reagent of general applicability has previously been found which is applicable to all types of substituted tetrahydrocarbazoles, and which gives the corresponding /

corresponding substituted carbazole readily, reasonably pure, and in good yield. If such a reagent is found, one of the numerous problems in the carbazole series will be solved, namely, the preparation in good yield of many mono-substituted carbazoles, and in particular of 1-substituted carbazoles. For example, 1-nitrocarbazole is obtained only in small yield in the direct nitration of carbazole when the main product is 3-nitrocarbazole, the 3- position being reactive in para position to the imino group. Tucker and co-workers (J.1942, 500) have increased the yield of 1-nitrocarbazole obtained by this method to 6%, by chromatographic separation from the 3-isomer. They were also successful in effecting the conversion of 7-nitro-1-phenyl-1:2:3-benztriazole into 1-nitrocarbazole in 18% yield, a conversion which had hitherto not been found possible. Finally, they obtained a 38% yield of 1-nitrocarbazole by decarboxylation of 1-nitro-carbazole-3:6-dicarboxylic acid . However, 8-nitro-1:2:3:4-tetrahydrocarbazole, readily prepared from o-nitrophenylhydrazine and cyclohexanone, offers a rich source of 1-nitrocarbazole, a very important derivative in the carbazole series, if a suitable oxidising agent can be found.



Recently, Arnold and Collins published their results of work on the low-temperature dehydrogenation /

dehydrogenation of hydroaromatic rings (J.A.C.S.1939, 61, 1407). The reagent used was chloranil in boiling xylene and was found to be effective in a large number of cases. For example, 9:10-dihydroanthracene was oxidised to anthracene in 63% yield after 33 hours, phenylcyclohexene was oxidised to biphenyl in 52% yield after 4 hours, and many other successful oxidations are listed. In a later paper (J.A.C.S.1940, 62, 983), Arnold, Collins and Zenk reported further work and mentioned that groups such as $-NO_2$ were unaffected by the dehydrogenation reaction with chloranil, although they are affected when sulphur or selenium is used. This reagent used at low temperature seemed efficient and yet mild in that it did not affect other groups present in the molecule, and this property indicates that it might be a suitable reagent for the dehydrogenation of substituted tetrahydrocarbazoles.

It therefore seemed of value to investigate the possibility of obtaining substituted carbazoles, and in particular derivatives which had not previously been prepared, by chloranil dehydrogenation of substituted tetrahydrocarbazoles.

OBJECT OF RESEARCH.

The main object of this research was, therefore, the preparation of substituted carbazoles by dehydrogenation of substituted hydrocarbazoles, and in particular of substituted tetrahydrocarbazoles, using chloranil in boiling xylene as the reagent for the dehydrogenation.

Success in the preparation of substituted carbazoles by this method was dependent not only on the successful application of the dehydrogenation process, but also on three other factors :-

(1) the preparation of pure substituted phenylhydrazines.

(2) improved methods of condensation of phenylhydrazines with cyclohexanone.

(3) improved methods of ring closure of the cyclohexanone phenylhydrazones to substituted tetrahydrocarbazoles.

Each of these factors required investigation and the results of these investigations are dealt with in detail in the experimental section and in the discussion of experimental results.

EXPERIMENTAL SECTION - INTRODUCTION.

The experimental work carried out in the course of the research is described in the following pages. Yields of products are qouted as percentages of the maximum theoretical amounts obtainable. Melting points were determined on the apparatus described in "Qualitative Organic Chemistry" by Neil Campbell (see p.7, fig.4) , and were checked for sharpness on a micro melting-point apparatus (Kofler, Mikrochem. 1934, 15, 242).

All new compounds obtained in the pure state were analysed by micro methods by Drs. Weiler and Strauss of Oxford, or by Mr. A. MacDonald of the Heriot-Watt College, Edinburgh.

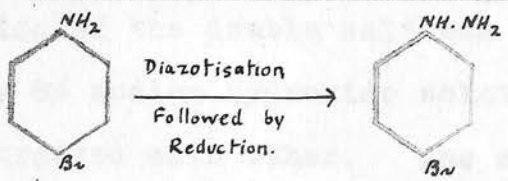
EXPERIMENTAL.

As the method of obtaining the substituted carbazoles is essentially the same in all cases, one example is given in detail, namely the preparation of 3-bromocarbazole, from the preparation of the required substituted phenylhydrazine to the final isolation and purification of the substituted carbazole. For the other compounds, any differences in preparation and isolation of the various stages in the complete syntheses of these compounds are noted.

I

Preparation of 3-bromocarbazole.

1st stage : preparation of p-bromophenylhydrazine.

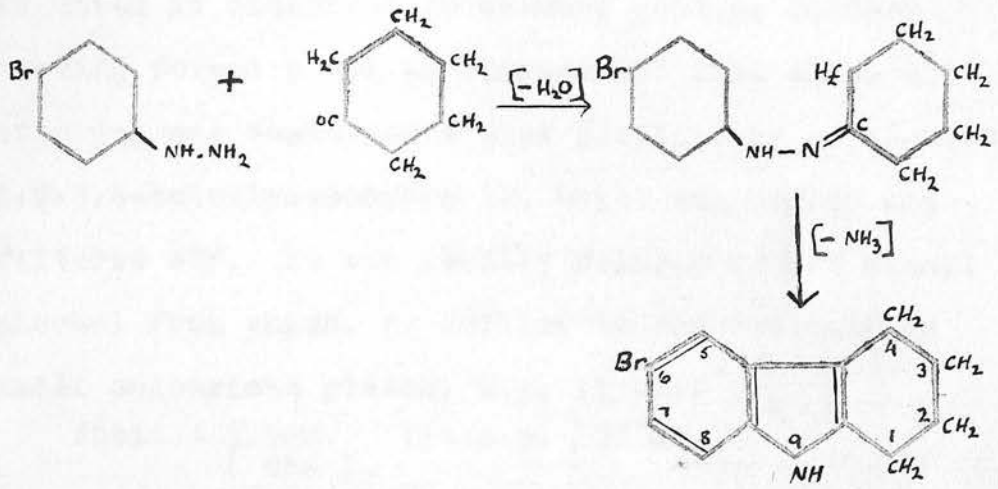


Several attempts to prepare p-bromophenylhydrazine by the somewhat similar methods of Coleman (Organic Syntheses, Vol.2, 71) and Davies (J.1922, 121, 717), by reduction of the p-bromobenzenediazonium chloride with sodium sulphite solution, were unsuccessful, although in each case a very small quantity of the p-bromophenylhydrazine hydrochloride was isolated. Finally, the following method of Bülow (Ber.1918, 51, 404) was tried and found to be highly satisfactory, giving a good yield of clean, crystalline p-bromophenylhydrazine.

P-bromoaniline (21.5 gm.) was dissolved in 200 c.c. warm dilute hydrochloric acid; the warm solution was added to 320 c.c. of stirred concentrated hydrochloric acid, so that a fine precipitate of the hydrochloride of the base separated. The mixture was cooled to about 0°C, and diazotised with 50 c.c. of a 20% sodium nitrite solution. A clear diazo-solution was obtained, to which was quickly added an ice-cold solution of 64 gm. stannous chloride in 80 c.c. concentrated hydrochloric acid. The thick mass of double salt which separated immediately was allowed to stand for 2-3 hours , after which time it was filtered, well washed with a saturated sodium chloride solution, and pressed fairly dry. Decomposition of the double salt was readily effected by 8% sodium hydroxide solution, and the mixture extracted with ether. The ethereal solution of the p-bromophenylhydrazine so obtained was dried over anhydrous sodium sulphate, and on evaporation yielded 18 gm. of p-bromophenylhydrazine which crystallised from hot water in colourless needles .

Yield = 78% . m.p. 107°C.
lit.m.p. 108°C.

2nd stage : condensation of cyclohexanone and p-bromophenylhydrazine, and subsequent cyclisation of the cyclohexanone p-bromophenylhydrazone to 6-bromo-1:2:3:4-tetrahydrocarbazole.



Several small-scale condensations were attempted, by which it was proved advisable not to have present an excess of either reactant, and so reactants were weighed correct to two decimal places on an ordinary macro balance.

P-bromophenylhydrazine (3.03 gm.) was added to cyclohexanone (1.59 gm.), and the mixture warmed gently over a small flame until the hydrazine melted; the mixture became uniform and water was given off. Immediately on cooling, the crystalline cyclohexanone p-bromophenylhydrazone separated; it crystallised from aqueous ethyl alcohol in fine, colourless needles. m.p. 49 - 50°C. Borsche, Witte and Bothe (Ann.1908, 359, 66) give no m.p. for the hydrazone, which was found to decompose fairly quickly in air in the pure state, although it seemed to be reasonably stable in the crude state. The cyclohexanone p-bromophenylhydrazone was at once added to 50 c.c. dilute sulphuric acid (1:9 by vol.) in /

in which it dissolved on warming gently; further heating formed a "milky suspension" from which on stirring was deposited a fine precipitate of 6-bromo-1:2:3:4-tetrahydrocarbazole, which was cooled and filtered off. It was readily soluble in hot methyl alcohol from which, on cooling it crystallised in small colourless plates. m.p. 151-152°C.

Yield = 3.5gm. (88%). lit.m.p. 153°C.

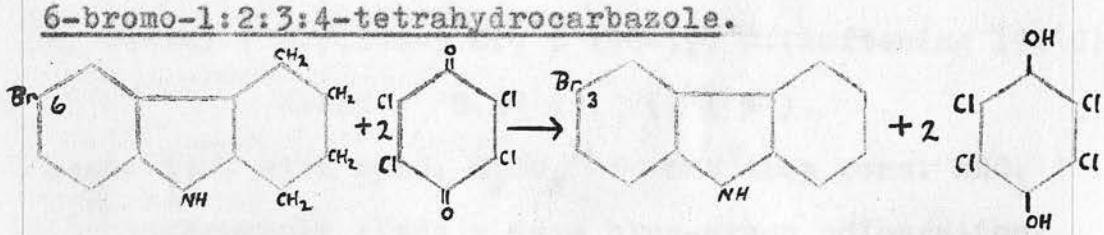
Picrate of 6-bromotetrahydrocarbazole : orange-red elongated prisms (alcohol). m.p. 133 - 134°C.

Analysis : N fd. = 12.35 %.

$C_{18}H_{15}N_4BrO_7$ requires N = 11.7 %.

The high figure for N is probably accounted for by the fact that the picrate decomposes, and therefore a higher proportion of picric acid was probably present in the sample analysed.

3rd stage : action of chloranil in boiling xylene on 6-bromo-1:2:3:4-tetrahydrocarbazole.



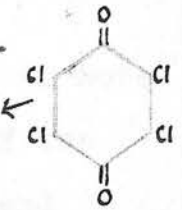
0.82 gm. 6-bromo-1:2:3:4-tetrahydrocarbazole.

1.61 gm. of chloranil.

15 c.c. sulphur-free xylene.

The reaction mixture was refluxed for 18 hours and cooled. Tetrachlorohydroquinone (1.5 gm.) was separated by filtration. After crystallisation from glacial acetic acid, it was identified by m.p., and /

and mixed m.p. with a sample of tetrachlorohydroquinone prepared by reducing chloranil with sulphur dioxide.



On standing, the filtrate deposited 0.3 gm. of clean crystals m.p. 194-196°C, which was not appreciably raised by repeated recrystallisation from alcohol. (3-bromocarbazole melts at 199°C.).

The filtrate from these crystals was diluted with an equal volume of ether, and the extract washed with a 4% aqueous potassium hydroxide solution to remove the last traces of tetrachlorohydroquinone, washed with water, dried over anhydrous sodium sulphate, and evaporated to small volume, when a further 0.28 gm. of oxidation product was deposited. Crystallisation from ethyl alcohol (charcoal) gave small colourless prisms. m.p. 198 - 199°C. Mixed m.p. with a specimen kindly supplied by Dr. Tucker (m.p.194-5°C.) : 196-197°C.(softening 194°C).

Yield : 0.58 gm. (71 %).

Colour test with conc. H_2SO_4 + one drop conc. HNO_3 : 3-bromocarbazole gives a deep blue-green colouration.

It should be noted that at least 90 % of tetrachlorohydroquinone has been recovered in this experiment, although, included in the 1.5 gm. noted above, is a small residue (about 0.05 gm.) which does not melt up to 280°C, and is very insoluble in all the usual solvents. These properties suggest a substituted dicarbazyl which might be formed in the course of the oxidation, but it was not further /

further investigated.

It is advantageous at this point to note one or two modifications which were made of the original experimental procedure of Arnold and Collins (J.A.C.S.,1939, 61, 1407). These authors observed a slight oxidation of the solvent over long periods of reflux, and for this reason a 5-10% excess of chloranil was used. In the experiments with tetrahydrocarbazoles , such an oxidation of the solvent was not observed, and the best results were obtained when no excess of the quinone over the two molecular proportions required was used ; the presence of excess unused quinone introduced complications in the working up of the reaction mixture at the end of the reflux period. It was also found that a cleaner mixture was obtained when sulphur-free xylene was used instead of ordinary commercial xylene (b.p.140°C), the solvent employed by the above authors. The amount of sulphur-free xylene used was the minimum volume required of boiling solvent to dissolve the reactants.

// Preparation of 1-bromocarbazole.

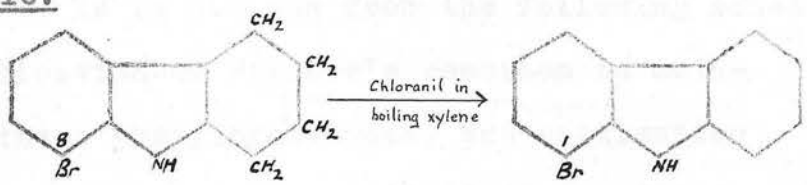
O-bromophenylhydrazine was prepared in good yield from o-bromoanailine by the method of Bűlow already described, and crystallised from hot water in colourless needles . m.p. 46-47°C.

lit. m.p. 48°C.

Test condensation : 1 gm. of the o-bromophenylhydrazine was heated gently for a few minutes over a small flame with 0.53 gm. of cyclohexanone until water was given off. The solution, when cooled and scraped with a glass rod, deposited a solid cyclohexanone o-bromophenylhydrazone, which crystallised from methyl alcohol in small colourless needles m.p.51-52°C. A mixed m.p. with o-bromophenylhydrazine was 45-50°C, showing that condensation had occurred. On treatment with dilute sulphuric acid (1:9 by volume) , the hydrazone dissolved, and on further warming the solution became milky ; finally a dark-reddish oily layer separated. Even after washing several times with water, the oily layer did not crystallise, but remained as a semi-solid oil which was assumed to be 8-bromo-1:2:3:4-tetrahydrocarbazole.

Repeat condensation on large scale : the cyclohexanone o-bromophenylhydrazone required to be warmed on the water-bath for some time with the dilute sulphuric acid, and eventually deposited a heavy viscous oil which was washed twice with water, dissolved in methyl alcohol and ether added. The ether was allowed to evaporate at room temperature, and as no crystals appeared, the methyl alcohol was also evaporated at room temperature, leaving a good yield of a thick semi-solid oil which was assumed to be the 8-bromo-1:2:3:4-tetrahydrocarbazole.

Action of chloranil on 8-bromo-1:2:3:4-tetrahydrocarbazole.



This was carried out twice according to the instructions given for the oxidation of 6-bromotetrahydrocarbazole, the period of reflux being 21.5 hours. In each case at least an 87% yield of 1-bromocarbazole was obtained, though the product was somewhat sticky. It was purified first by triturating with benzene, leaving a fairly clean precipitate , m.p.104-106°C, which was dissolved in benzene and chromatographed through a short column of alumina leaving a narrow dirty ring at the top of the chromatogram. Four portions (30 c.c.each) of the benzene eluate were evaporated giving clean precipitates, which were again triturated with benzene. m.p. of 1-bromocarbazole so obtained, 111-112°C.

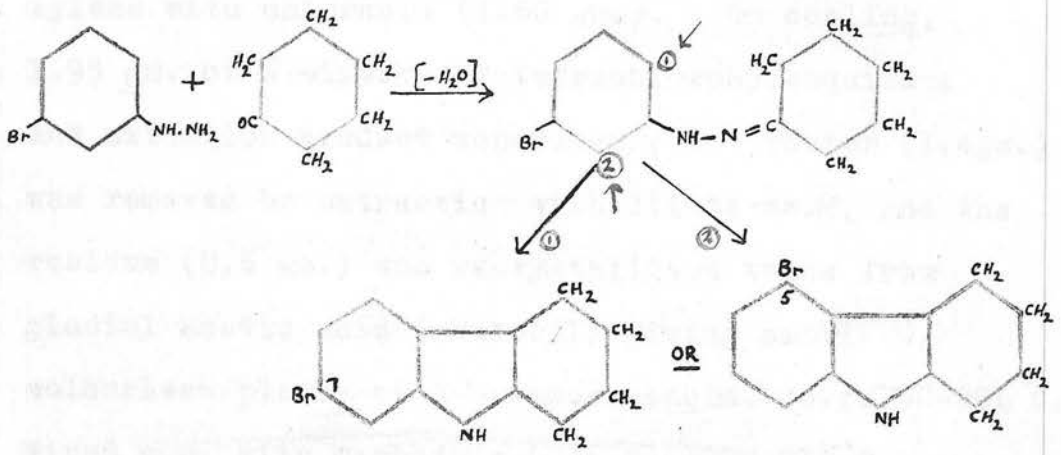
Analysis : Br Fd. = 32.2 %.
$C_{12}H_8NBr$ requires Br = 32.5%,

Note : although the figure 32.2% also agrees with that of 31.97%, the bromine figure for the bromotetrahydrocarbazole, it can be assumed that the compound analysed was indeed 1-bromocarbazole, since as a result of the action of chloranil on the 8-bromotetrahydrocarbazole, the quantitative amount of tetrachlorohydroquinone was recovered, showing that oxidation has occurred.

Colour test: with conc.H_2SO_4 + 1 drop conc. HNO_3: 1-bromocarbazole gives an intense bottle-green.

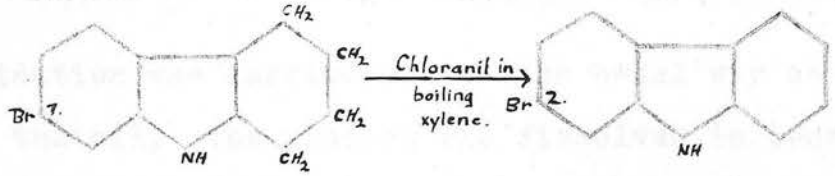
/// Preparation of 2-bromocarbazole and 4-bromocarbazole.

As is obvious from the following scheme, in application of Fischer's reaction to meta-substituted phenylhydrazones, the cyclisation process can occur in two distinct positions, and a mixture of substituted tetrahydrocarbazoles may be expected to result :



M-bromophenylhydrazine was prepared in good yield in this department (by Mr. Gow) by Bülow's method, and used to prepare a mixture of 5- and 7-bromo-1:2:3:4-tetrahydrocarbazoles according to the instructions of Plant and Wilson (J.1939, 237). 7-bromotetrahydrocarbazole (m.p. 183°C with decomposition) was obtained by alcoholic extraction of the semi-solid product from dilute sulphuric acid treatment of the cyclohexanone m-bromophenylhydrazone. The alcoholic filtrate was assumed to contain mainly 5-bromotetrahydro-carbazole and was retained for oxidation with chloranil after evaporation to dryness (see p.22).

(a) Action of Chloranil on 7-bromo-1:2:3:4-tetrahydrocarbazole.



7-bromo-1:2:3:4-tetrahydrocarbazole (0.85 gm.) was refluxed for 24 hours in 15 c.c. sulphur-free xylene with chloranil (1.66 gm.). On cooling, 1.95 gm. of a mixture of tetrachlorohydroquinone and oxidation product separated ; the former (1.4gm.) was removed by extraction with dilute NaOH, and the residue (0.5 gm.) was recrystallised twice from glacial acetic acid (charcoal) giving small colourless plates of 2-bromocarbazole. m.p.250-251 °C. Mixed m.p. with carbazole (246 °C), 230-233 °C., softening from 220 °C.

The xylene filtrate was diluted with an equal volume of ether, and the remainder of the tetrachlorohydroquinone removed by basic extraction. On evaporation, a further 0.275 gm. of product was obtained, containing a small amount (0.05 gm.) of a high-melting, very insoluble residue, which was removed when the 2-bromocarbazole was chromatographed in benzene. Finally, the 2-bromocarbazole was recrystallised from glacial acetic acid. m.p. as above. Yield : 0.725 gm. (85 %). Analysis : Br fd.= 32.4 %.

$C_{12}H_8NBr$ requires Br = 32.5 %.

Colour test : with conc. H_2SO_4 + 1 drop conc. HNO_3 : 2-bromocarbazole gives an intense blue-green colour.

(b) Action of Chloranil on oil assumed to contain mainly 5-bromo-1:2:3:4-tetrayhdrocarbazole.

Oxidation was carried out in the usual way on 2.58 gm. of the oil; the product was dissolved in benzene and chromatographed (alumina, 18x¾ inch) with benzene followed by a 3:1 mixture of benzene and light petroleum (100-120°C.) as elution agents. The eluate was tested with conc. H_2SO_4 + 1 drop conc. HNO_3 at intervals, and collected until the characteristic intense blue-green colour was no longer observed. The numerous extracts were evaporated to small volume; in all cases crystals melting from 245° to 250°C were obtained, which gave a depression with carbazole, and which on recrystallisation from glacial acetic acid (once) melted at 249-251°C (see(a) above).
2-bromocarbazole has again been obtained (the 4-isomer melts at 104-105°C. - see p. 25) , and no trace of 4-bromocarbazole as was to be expected if the above oil had contained 5-bromo-1:2:3:4-tetrahydrocarbazole.

It was therefore decided to repeat the preparation of the mixture of the bromotetrahydrocarbazoles, and with a view to obtaining cleaner products, a slight modification of the original procedure for the cyclisation of the cyclohexanone m-bromophenylhydrazone was adopted. A mixture of 30 c.c. conc. H_2SO_4 , 100 c.c. alcohol, and 170 c.c. water /

water was added to the hydrazone prepared from m-bromophenylhydrazine (17 gm.) and cyclohexanone (11 gm.), and the whole warmed until complete solution was obtained. 5.5 gm. clean crystals (A), decomposing 150°C., separated from the cold solution. As it was thought this might be a molecular compound of the 5- and 7-bromotetrahydrocarbazoles, 1 gm. was chromatographed (alumina) in benzene, but only one product was obtained, and that quantitatively. It melted with decomposition about 180°C. after one crystallisation from a mixture of methyl and ethyl alcohol, and therefore was 7-bromo-1:2:3:4-tetrahydrocarbazole.

The filtrate from (A) was warmed and 50 c.c. warm water added; on cooling, a further 1 gm. of 7-bromo-1:2:3:4-tetrahydrocarbazole was obtained and filtered off. A large volume of water was added to the filtrate, until a heavy oily layer was deposited. This was separated , taken up in ether, the ether solution well washed with water to remove alcohol, and finally dried over anhydrous sodium sulphate. One third (by volume) of the ether solution was evaporated to dryness and the semi-solid obtained weighed and treated with chloranil.

Action of Chloranil on semi-solid assumed to contain 5-bromo-1:2:3:4-tetrahydrocarbazole.

Bromotetrahydrocarbazole (2.88 gm.) was refluxed for 24 hours with chloranil (5.66 gm.) in 50 c.c. sulphur-free /

free xylene. 85 % of the tetrachlorohydroquinone was recovered. On evaporation of two-thirds of the xylene, 0.24 gm. of crystals separated which, after crystallisation once from glacial acetic acid, melted at 247-248°C ; they gave a depression with carbazole, but not with the 2-bromocarbazole already prepared. The xylene filtrate from these crystals was evaporated to dryness giving a further 2.10 gm. of product . The total yield of crude oxidation product was therefore 2.34 gm. (81%).
2.10 gm. were dissolved in benzene (25 c.c.) and chromatographed (alumina, 18 × 0.75 inch.) using as elution agent a 3:1 mixture of benzene and light petroleum (100-120°C.). The eluate was tested in the usual way with conc. H_2SO_4 + one drop conc. HNO_3 , and 30 c.c. portions of eluate collected until the result of the colour test was only a very faint blue-green colouration. Eight 30 c.c. portions in all were collected and allowed to evaporate. Portions one, two and three on evaporation gave very small amounts of a high-melting, yellow, very insoluble by-product, which again may be a substituted dicarbazyl, but was not further investigated. Portions four to eight gave a total of 1.17 gm. of a product melting about 100°C., and which was very much more soluble in glacial acetic acid than is 2-bromocarbazole. It was purified by several /

several recrystallisations from aqueous methyl alcohol . m.p. of 4-bromocarbazole so obtained :

104-105°C.

Analysis : Br fd. = 33.2 %.

$C_{12}H_8NBr$ requires Br = 32.5 %.

Colour test : with conc.H_2SO_4 + 1 drop conc. HNO_3 : 4-bromocarbazole gives an intense bottle-green.

IV Preparation of 3-chlorocarbazole.

Due to the impure state of the p-chloro-aniline and the small quantity available at the time , only 1.3 gm. of p-chlorophenylhydrazine were obtained by the usual method . It was immediately condensed with 0.91 gm. of cyclohexanone and the hydrazone treated with dilute H_2SO_4 (1:9 by volume) giving the 6-chloro-1:2:3:4-tetrahydro-carbazole in good yield. It crystallised in elongated prisms from alcohol (twice)

m.p. 143-144°C.

cf. Borsche, Witte and Bothe (Ann.1908, 359, 66) give the m.p.of 6-chloro-1:2:3:4-tetrahydrocarbazole as 138°C .

Action of Chloranil on 6-chloro-1:2:3:4-tetrahydro-carbazole : 6-chlorotetrahydrocarbazole (0.61 gm.) was refluxed for 24 hours with chloranil (1.46 gm.) in 15 c.c. of sulphur-free xylene. Tetrachloro-hydroquinone was recovered in almost quantitative yield. The xylene liquor, after the usual treatment, deposited a total yield of 0.3 gm.(50%)

of /

of 3-chlorocarbazole which crystallised from glacial acetic acid in glistening flakes. m.p. 199-200°C.
lit. m.p. 201.5°C.

Colour test: with conc.H_2SO_4 + 1 drop conc.HNO_3 : 3-chlorocarbazole gives an intense green colour. Again, a very small amount of a high-melting, very insoluble by-product was obtained, and was found to give the intense blue-green colour with conc.H_2SO_4 + 1 drop conc.HNO_3 . This observation would fit with the suggestion already advanced that these by-products in the chloranil oxidations may be substituted dicarbazyls.

V Preparation of 1-chlorocarbazole.

O-chlorophenylhydrazine was obtained in good yield by the usual method. m.p.(crude) 45-47°C.
lit. m.p. 48°C.

O-chlorophenylhydrazine (3.8 gm.) was warmed gently with cyclohexanone (2.61 gm.) until a homogeneous solution was obtained; on cooling the solution, a crystalline cyclohexanone o-chlorophenylhydrazone was deposited. m.p. 51-52°C. cf. Borsche, Witte and Bothe (Ann.1908, 359, 65) give no m.p. for the phenylhydrazone. The phenylhydrazone gave a depression with the original o-chlorophenylhydrazine, showing that condensation had actually occurred. On warming gently for a few minutes with dilute sulphuric acid (1:9 by volume), the hydrazone /

hydrazone dissolved and finally the milky solution deposited 3.28 gm. (quantitative yield) of a somewhat "sticky" 8-chloro-1:2:3:4-tetrahydrocarbazole. It was washed well with water, dried thoroughly, and recrystallised first from light petroleum (b.p.60-80°C.), then from a mixture of benzene and light petroleum (80-100°C.) giving colourless prisms m.p.54-55°C. lit.m.p. 55-56°C.

Action of Chloranil on 8-chloro-1:2:3:4-tetrahydrocarbazole: 8-chlorotetrahydrocarbazole (0.47 gm.) was refluxed for 24 hours with chloranil (1.12gm.) in 15 c.c. sulphur-free xylene. 94% of tetrachlorohydroquinone was recovered, and 89% of crude oxidation product, m.p.90-95°C., was isolated. It was purified by repeated recrystallisation from aqueous methyl alcohol until the m.p.was constant. 1-chlorocarbazole (plates or prisms from aqueous methyl alcohol) : m.p.109-110°C.

(The only m.p. quoted for 1-chlorocarbazole is 125°C., given in Chem.Zentr., 1931, 2, 2215, where a method is given for the preparation of 1-chlorocarbazole by removal of $-SO_3H$ groups from 1-chlorocarbazole-3:6:8-trisulphonic acid.)

Analysis : Cl fd. = 13.39 %.

$C_{12}H_8NCl$ requires Cl = 13.98 %.

Colour test: with conc.H_2SO_4 + 1 drop conc.HNO_3 : 1-chlorocarbazole gives an intense blue-green colour.

VI Preparation of 1:4-Dichlorocarbazole.

2:5-Dichlorophenylhydrazine (3 gm.-B.D.H.) condensed very readily when shaken with cyclohexanone (1.67 gm.) in 20 c.c. alcohol to give cyclohexanone 2:5-dichlorophenylhydrazone in small white prisms . m.p. 65°C.

Analysis: Cl fd. = 10.89 %.

$C_{12}H_{14}N_2Cl_2$ requires Cl = 10.90 %.

The hydrazone was refluxed for one hour with ten times its weight of dilute sulphuric acid (1:9 by vol.), in which it melted and formed a yellow oil which on further heating darkened to reddish-brown. On cooling the mixture, a semi-solid product was obtained, m.p. 80-90°C. An aqueous methyl alcoholic solution of a small fraction of the product gave, on cooling, a very tarry precipitate, so the main bulk of the product was dissolved in methyl alcohol and refluxed for a further two and a half hours with 25 c.c. of dilute sulphuric acid giving a dark reddish-brown oil which solidified on cooling. The solid so obtained was thoroughly dried and ground to a light brown powder, which, after a further recrystallisation from aqueous methyl alcohol, melted at 85°C. By repeated extraction with methyl alcohol, and reprecipitation with warm water, pure white (opaque) prisms of 5:8-dichloro-1:2:3:4-tetrahydrocarbazole were obtained. m.p.90-92°C.

As the conversion of the dichlorophenylhydrazone /

hydrazone to the tetrahydrocarbazole by dilute sulphuric acid had been somewhat difficult, and the purification of the tetrahydrocarbazole tedious and not altogether satisfactory, it was decided to attempt the cyclisation process by use of a 50-50 mixture of ethyl alcohol and conc. hydrochloric acid, (a) by heating the hydrazone directly with this mixture, and (b) by refluxing the hydrazone on the water-bath for a longer period with the mixture. Im both cases, the product was no cleaner than when dilute sulphuric acid was used for the cyclisation, so it was decided to repeat the preparation of the 5:8-dichlorotetrahydrocarbazole and attempt to purify it by chromatographic analysis.

The product from dilute sulphuric acid treatment was extracted thrice with light petroleum (60-80°C.), the extracts allowed to evaporate, and the residues so obtained taken up in benzene and washed through a short column of alumina (12 × ½ inch). Four portions of benzene eluate were collected and allowed to crystallise; the 5:8-dichlorotetrahydrocarbazole was again recrystallised from aqueous methyl alcohol in white prisms m.p. 91-93°C.

Analysis : N fd. = 5.84% ; Cl fd. = 28.71, 28.92 %.

$C_{12}H_{11}NCl_2$ requires N = 5.87 % ; Cl = 29.55 %.

Action of Chloranil on 5:8-dichlorotetrahydrocarbazole.

Several oxidations with chloranil were carried out in the usual way on the samples of 5:8-dichlorotetrahydro-carbazole /

carbazole obtained by the various cyclisation processes, the cleanest experiment being the oxidation of dichlorotetrahydrocarbazole which had been purified by the chromatographic method.
5:8-Dichlorotetrahydrocarbazole (2.45 gm.) was refluxed for 10 hours with chloranil (4.78 gm.) in 40 c.c. sulphur-free xylene. 88% of the tetrachlorohydroquinone was recovered, and at least 75% of crude 1:4-dichlorocarbazole was obtained. The latter was purified by washing through a column of alumina followed by repeated recrystallisation from aqueous methyl alcohol 84-85°C. m.p.
Analysis : Cl fd. = 29.27 %.
$C_{12}H_7NCl_2$ requires Cl = 30.05 %.
Colour test: with conc.H_2SO_4 + 1 drop conc. HNO_3 : 1:4-dichlorocarbazole gives an intense green colour.

VII Preparation of 1-methylcarbazole.
o-Tolylhydrazine (15 gm. - B.D.H.) readily condensed with cyclohexanone (13 gm.) to give cyclohexanone o-tolylhydrazone, needles from methyl alcohol ,
m.p. 62-64°C .
Analysis : N fd. = 9.96%.
$C_{13}H_{18}N_2$ requires N = 13.82%. The hydrazone decomposed rapidly.
Cyclisation was effected by refluxing the hydrazone for 6 hours on the water-bath with dilute sulphuric acid (1:9 by volume) . The 8-methyl-1:2:3:4-tetrahydrocarbazole crystallised from methyl alcohol in /

in almost colourless gleaming plates . m.p. 97-98°C.

Analysis : N fd. = 7.30 %.

$C_{13}H_{15}N$ requires N = 7.56 %.

Picrate of 8-methyltetrahydrocarbazole : chocolate-brown needles (methyl alcohol) m.p.132-134°C.

Analysis : N fd. = 15.15 %.

$C_{19}H_{18}O_7N_4$ requires N = 13.53 %. The picrate showed signs of decomposition.

Action of Chloranil on 8-methyl-1:2:3:4-tetrahydro-carbazole.

8-methyltetrahydrocarbazole (1.5 gm.) was refluxed for 18 hours with chloranil (4 gm.) in 50 c.c. sulphur-free xylene. A 70 % yield of 1-methylcarbazole was obtained . It crystallised in plates from ligroin . m.p. 114°C.

lit. m.p. 120.5°C.

Picrate of 1-methylcarbazole : red needles (alcohol):

m.p. 145-147°C.

lit. m.p. 143.5°C.

Colour test: with conc. H_2SO_4 + 1 drop conc. HNO_3 : 1-methylcarbazole gives an intense green colour.

VIII Preparation of 3-methylcarbazole.

Cyclohexanone was condensed with p-tolylhydrazine hydrochloride (B.D.H.) in alcohol, in presence of sodium acetate in water. The reaction mixture was warmed gently for 2 hours in a low temperature oven, and allowed to stand overnight . The product, after

two /

two recrystallisations from methyl alcohol, melted at 141-142°C. 6-Methyl-1:2:3:4-tetrahydrocarbazole melts at 141-142°C , and therefore it was concluded that the above reaction mixture produced sufficient dilute mineral acid to effect the cyclisation to the tetrahydrocarbazole, since on heating the product with dilute sulphuric acid as usual, no further change had occurred , and the m.p. remained 141-142°C. The yield, however, was only 40%.

Analysis : Fd. N = 7.75 %.

$C_{13}H_{15}N$ requires N = 7.56 %.

Action of Chloranil on 6-methyl-1:2:3:4-tetrahydrocarbazole.

The period of reflux was 18 hours, and at least 50% of 3-methylcarbazole was obtained and after recrystallisation twice from alcohol (gleaming plates) melted at 199-202°C.

lit. m.p. 203°C.

Picrate of 3-methylcarbazole : red needles from alcohol:

m.p. 178-181°C.

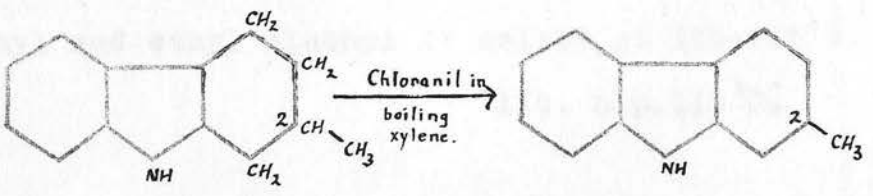
lit. m.p. 180°C.

Colour test: with conc. H_2SO_4 + 1 drop conc. HNO_3 : 3-methylcarbazole gives an intense blue-green colour.

IX Preparation of 2-Methylcarbazole.

M-methylcyclohexanone (15 gm.) was mixed with phenylhydrazine (15 gm.) and warmed gently, whereby a yellow curdy product was formed, which was immediately refluxed for 5 hours on the water-bath with 300 c.c. dilute sulphuric acid (1:9 by volume). A yellow oil which resulted was extracted with ether, and the ether solution dried over anhydrous sodium sulphate. The ether was evaporated and the product, a yellow oily solid, was purified by vacuum distillation . b.p. 180-200°C / 20 mm. The distillate solidified to a yellow mass, which on crystallisation from alcohol gave white crystals, m.p. 94°C. lit. m.p. 98-100°C.
The yield of pure product was, however, only 6 gm.
Picrate of 2-methyl-1:2:3:4-tetrahydrocarbazole : reddish-brown needles from alcohol . m.p. 148°C.
lit. m.p. 155°C.

In the above process two products are possible, namely, 2-methyl-1:2:3:4-tetrahydrocarbazole, and 4-methyl-1:2:3:4-tetrahydrocarbazole.
However, only one product was isolated and was proved to be the 2-methyl derivative, since on oxidation with chloranil it yielded 2-methylcarbazole.
Action of Chloranil on 2-methyl-1:2:3:4-tetrahydrocarbazole.



2-Methyl-1:2:3:4-tetrahydrocarbazole (1.5 gm.) was refluxed for 18 hours with chloranil (4 gm.) in 40 c.c. xylene. A good yield of 2-methylcarbazole was isolated in the usual way, and after recrystallisation (twice) from alcohol, gave colourless plates. m.p. 259°C. (lit.)

Analysis : fd. C = 84.8 %; H = 5.8 %.

$C_{13}H_{11}N$ requires C = 86.2 %; H = 6.1 %.

For confirmation, a picrate was prepared in alcohol: bright orange-red elongated prisms . m.p. 166°C.

lit. m.p. 167°C.

Analysis of Picrate: fd. N = 14.3 %.

$C_{19}H_{14}O_7N_4$ requires N = 13.7 %.

Colour test: with conc.H_2SO_4 + 1 drop conc. HNO_3 : 2- methylcarbazole gives an intense blue-green colour.

X Preparation of Carbazole.

Carbazole was prepared by oxidation of three different reduced carbazoles with chloranil in boiling xylene .

(a) oxidation of tetrahydrocarbazole.

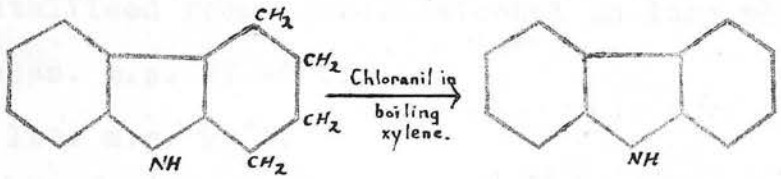
(b) oxidation of hexahydrocarbazole.

(c) oxidation of dihydrocarbazole.

(a) Tetrahydrocarbazole was prepared in good yield in the usual way from cyclohexanone and phenylhydrazine. After two recrystallisations from a 2:1 mixture of methyl and ethyl alcohol it melted at 115-116°C.

lit. m.p.116°C.

Action of Chloranil on Tetrahydrocarbazole.



The period of reflux was 24 hours. Carbazole so prepared was readily purified by recrystallisation from glacial acetic acid (charcoal), from which it crystallised in shiny plates.

m.p. 243-244°C.

lit. m.p. 246°C. Yield = quantitative.

No depression was given with an authentic specimen (B.D.H.).

Picrate : bright red needles (alcohol). m.p. 188°C.

lit. m.p. 186-7°C.

No depression was given with a sample of carbazole picrate prepared from B.D.H. carbazole.

Colour test :with conc. H_2SO_4 + 1 drop conc.HNO_3 : carbazole gives an intense blue-green colouration.

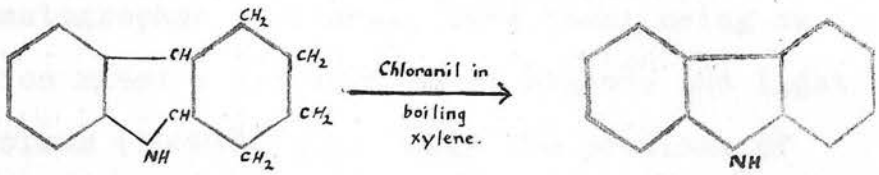
(b) Hexahydrocarbazole was prepared by reduction of tetrahydrocarbazole as follows :

Tetrahydrocarbazole (15 gm.) was refluxed for 4 hours on the water-bath with 10 c.c. ethyl alcohol, 15 c.c. concentrated hydrochloric acid and 10 gm. granulated tin. The mixture was filtered from undissolved tin, neutralised with sodium hydroxide solution, and distilled in steam. The hexahydro-carbazole /

carbazole (13 gm. - 85 %yield) so obtained crystallised from aqueous alcohol in long white needles. m.p. 97-98°C.

lit. m.p. 99°C.

Action of Chloranil on Hexahydrocarbazole :



One molecular proportion of hexahydrocarbazole was refluxed withthree molecular proportions of chloranil in sulphur-free xylene. The solution, which was originally dark in colour, became clear amber after a very short time, and as a precipitate separating in the hot solution after only 1½ hours reflux had the typical appearance of tetrachlorohydroquinone, the refluxing was stopped, and the solution cooled thoroughly. 94% of tetrachlorohydroquinone was recovered.
After two crystallisations from glacial acetic acid, a 70% yield of pure carbazole, m.p. 243-244°C., was obtained and confirmed by mixed m.p. with an authentic specimen, and by preparation of the picrate.

(c) Crude dihydrocarbazole was prepared in this laboratory (by Mr. Gow) by the method of Schmidt and Schall (Ber.1907, 40, 3226) by reduction of carbazole with sodium and amyl alcohol.
After one crystallisation from glacial acetic acid it melted at 220°C.(lit. m.p. 228-229°C.) .

1 gm. of the dihydrocarbazole (possibly still containing a little carbazole) was treated with 100 c.c. cold xylene leaving 0.35 gm. undissolved (m.p.229°C.). The cold xylene solution (containing 0.65 gm.) was chromatographed (alumina, 24×¾ inch) using as elution agent a 3:1 mixture of benzene and light petroleum (100-120°C.). Only the portions of eluate giving a positive colour test (intense blue-green with conc.H_2SO_4 + 1 drop conc.HNO_3) yielded crystals on evaporation, and after recrystallisation from glacial acetic acid, melted at 227°C.

Picrate of dihydrocarbazole: chocolate-brown needles (alcohol), m.p. 179-180°C.(lit.).

Cf. Carbazole picrate: bright orange-red needles (alcohol), m.p. 189°C. (lit.m.p. 186-187°C.).

Trinitrobenzene compound of dihydrocarbazole : bright red needles (alcohol), m.p. 188-189°C.

Analysis : fd. N = 14.6 %.

$C_{18}H_{14}O_6N_4$ requires N = 14.65 %.

Cf. Carbazole trinitrobenzene compound : orange-yellow needles (alcohol), m.p. 199.5°C. (lit.).

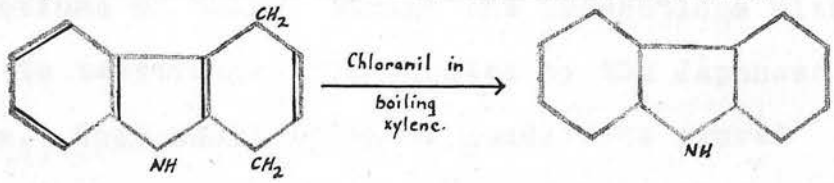
0.1 gm. of purified dihydrocarbazole was rechromatographed in the same way as above. Even then, taking very small portions of eluate, a positive colour test was shown by all portions yielding dihydrocarbazole, which was recrystallised twice from glacial acetic acid (charcoal) , and crystallised /

crystallised in colourless shiny plates. m.p. 231-232°C.
lit. m.p. 228-229°C.

Analysis : fd. C = 84.9 %; H = 5.78 %.

$C_{12}H_{11}N$ requires C = 85.2%; H = 6.64%.

Action of Chloranil on Dihydrocarbazole (twice) :



Equimolecular proportions of dihydrocarbazole and chloranil were refluxed for 24 hours in boiling xylene. The mixture was cooled thoroughly and worked up as before. 85% tetrachlorohydroquinone was recovered, and 83% carbazole isolated, which, after two recrystallisations from glacial acetic acid gave shiny plates m.p. 244-246°C. No depression of m.p. was shown with an authentic specimen of carbazole.

XI Preparation of 3-ethoxycarbazole.

1st stage: preparation of p-ethoxyphenylhydrazine.

Several attempts to prepare p-ethoxyphenylhydrazine by the method of Hoshino and Takiura (Bull.Chem.Soc.Japan, 1936, 218) proved unsatisfactory, although in each attempt some of the desired hydrazine was actually formed. The method is similar to that of Bülow, already used for the preparation of the halogenophenylhydrazines, except that the Japanese authors use /

use a very large excess of sodium nitrite solution in the diazotisation; also a large excess of stannous chloride and insufficient concentrated hydrochloric acid in the reduction . It was therefore decided to prepare the p-ethoxyphenylhydrazine according to the instructions of Bülow, taking the precautions with regard to temperature recommended by the Japanese authors. This combination of conditions proved satisfactory, and on evaporation of the ethereal solution of the hydrazine, an 80% yield of fairly clean plates, m.p.70-72°C., was obtained.

lit. m.p. 74°C.

2nd stage : condensation of p-ethoxyphenylhydrazine with cyclohexanone and subsequent cyclisation to 6-ethoxy-1:2:3:4-tetrahydrocarbazole.

P-ethoxyphenylhydrazine (15 gm.) was added to cyclohexanone (9.7 gm.) in which it dissolved; on shaking the solution, it became slightly warm and milky. The cyclohexanone p-ethoxyphenylhydrazone could not be induced to crystallise, so it was at once warmed with dilute sulphuric acid (1:9 by vol.) giving a loam solution containing an oily layer. The oily layer was decanted, dissolved in methyl alcohol, an equal volume of warm water added, and the mixture allowed to cool. 6-ethoxytetrahydrocarbazole (3gm.) was precipitated along with a semi-solid, which on repeated methyl alcoholic extraction and precipitation with /

with water gave a further 1.2 gm. of the tetrahydrocarbazole. The loam sulphuric acid solution on cooling also gave >1 gm.of clean crystals, and the total yield of >5 gm. was again recrystallised from methyl alcohol in clean needle-prisms, m.p. 102-104°C.

lit. m.p. 105-106°C.

3rd stage: Action of Chloranil on 6-ethoxy-1:2:3:4-tetrahydrocarbazole.

In this case a long period of reflux was found to be disadvantageous, producing a product which required considerable purification, along with a greenish-yellow, high-melting, insoluble by-product.

Finally, it was shown that a one-hour reflux with chloranil in boiling xylene was sufficient to complete the oxidation - after one hour no sign of unchanged chloranil was evident on testing with sodium hydroxide solution (chloranil on boiling with sodium hydroxide forms the sodium salt of chloranilic acid, which is deposited in red needles).

Tetrachlorohydroquinone was recovered in quantitative yield, and a 90% yield of crude 3-ethoxycarbazole was obtained. It was purified by chromatographing in benzene (alumina), using a 3:1 mixture of benzene and light petroleum (100-120°C.) as elution agent, and gave clean flaky crystals m.p. 103-105°C., which on recrystallisation from 50% methyl alcohol melted /

melted at 105 -106°C. lit. m.p. 106-107°C.
A mixed m.p. with 6-ethoxy-1:2:3:4-tetrahydrocarbazole gave a large depression, showing that 3-ethoxycarbazole had indeed been obtained .

Analysis : fd. N = 6.38 %.

$C_{14}H_{13}NO$ requires N = 6.64 %.

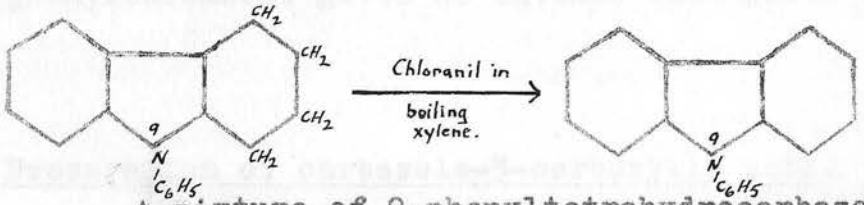
Colour test: with conc.H_2SO_4 + 1 drop conc.HNO_3: 3-ethoxycarbazole gives a dark greenish-brown colour.

XII Preparation of 9-Phenylcarbazole.

9-Phenyltetrahydrocarbazole was prepared in this laboratory (by Dr.Campbell) by the method of Linnell and Perkin (J.1924,125,2451). It crystallised from methyl alcohol in colourless compact prisms or elongated prisms, depending on the rate of crystallisation . m.p. 86-87°C.

lit. m.p. 88-89.5°C.

Action of Chloranil on 9-phenyltetrahydrocarbazole.



A mixture of 9-phenyltetrahydrocarbazole (0.517 gm.) and chloranil (1.03 gm.) was refluxed for 24 hours in 15 c.c. sulphur-free xylene. Tetrachlorohydroquinone was recovered quantitatively, and a 95% yield of crude oxidation product was isolated. It was first triturated with cold ethyl alcohol /

alcohol then recrystallised from ethyl alcohol (charcoal), giving colourless needles m.p. 87-89°C.

lit. m.p. 94-95°C.

Mixed m.p. with 9-phenyltetrahydrocarbazole (86-7°C.sharp): softening over a wide range and melting mainly 81-85°C. Therefore, although the depression in m.p. is not very large, the mixed m.p. showed a very wide range compared to the sharp m.p. of each component. The oxidation product is therefore 9-phenylcarbazole.

Picrate of 9-phenylcarbazole : bright red needles (alcohol), m.p. 128-129°C.

lit. m.p. 126-129°C.

Mixed m.p. with picric acid (122°C.) : 108-114°C. In this oxidation, no trace of any high-melting, very insoluble by-product was found, as in some other experiments. The significance of this observation will be mentioned in the discussion.

Colour test : with conc. H_2SO_4 + 1 drop conc.HNO_3: 9-phenylcarbazole gives an intense blue-green colour.

XIII Preparation of carbazole-3-carboxylic acid.

1st stage : preparation of p-carboxyphenylhydrazine: P-hydrazinobenzoic acid was prepared in good yield by a modification of the method of Bulow, used for the preparation of the halogeno-hydrazines. P-aminobenzoic acid was diazotised and the diazonium salt reduced with stannous chloride solution in the usual /

usual way. The tin double salt so obtained was decomposed with 2N NaOH, in which the free carboxyphenylhydrazine then dissolved. It was precipitated by carefully making the solution just acid with glacial acetic acid, filtered off, washed with cold water, and recrystallised from boiling water (charcoal) . m.p. 217 -220°C.(decomposition).

lit. m.p. 220-225°C.

2nd stage : condensation of p-hydrazinobenzoic acid with cyclohexanone and subsequent conversion of the cyclohexanone p-carboxyphenylhydrazone to 6-carboxy-1:2:3:4-tetrahydrocarbazole.

Condensation was finally achieved by heating equimolecular proportions of cyclohexanone and p-hydrazinobenzoic acid together, at first gently over a small flame (to avoid decomposition of the acid before reaction with cyclohexanone could occur), then more strongly until a uniform melt was obtained . On cooling the mixture, a glassy solid was obtained which was ground up before further treatment.

m.p.(without recrystallisation) 226-230 ° C.

lit. m.p. 236°C.

A mixed m.p. with a sample of the p-hydrazinobenzoic acid gave a large depression, showing that condensation had indeed occurred.

The powdered hydrazone was at once heated with ten times its weight of sulphuric acid (1:5 by volume - compare previous experiments in which 1:9 sulphuric acid used for cyclisation) in which it dissolved. The solution, on further heating became milky and finally deposited a fine precipitate of the 6-carboxy-1:2:3:4-tetrahydrocarbazole. It was crystallised once from aqueous ethyl alcohol (charcoal) giving almost colourless plates m.p. 268-272°C.
Collar and Plant (J.1926, 808) obtained 6-carboxy-tetrahydrocarbazole as colourless plates from aqueous ethyl alcohol , m.p. 282°C.

3rd stage : Action of Chloranil on 6-carboxy-1:2:3:4-tetrahydrocarbazole:

6-carboxy-1:2:3:4-tetrahydrocarbazole (0.3 gm.) was refluxed with chloranil (0.69 gm.) in 15 c.c. of sulphur-free xylene for 24 hours. From the subsequent treatment of this experiment, it was apparent that the 3-carboxycarbazole is even more insoluble in xylene than is tetrachlorohydroquinone, as much of the acid appeared in the first precipitate obtained on cooling the reflux mixture (proved by colour test and m.p.). The xylene liquor on evaporation deposited a mixture of the remainder of the acid, and a large proportion of the tetrachlorohydroquinone. It was therefore obvious that the oxidation with chloranil had been successful, and had not affected the -COOH group.

The /

The main difficulty lay in obtaining the carbazole acid free from tetrachlorohydroquinone (compare previous experiments in which tetrachlorohydroquinone was removed by basic extraction).

Two methods are possible :-

(1) At the end of the reflux period, distil off most of the xylene, and so precipitate completely a mixture of the carbazole acid and tetrachlorohydroquinone. Dissolve the mixture in NaOH, and pass in carbon dioxide to reprecipitate the carbazole acid.

(2) Prepare (e.g.) the ethyl ester of the tetrahydrocarbazole-carboxylic acid and oxidise it with chloranil, thus obtaining the ethyl ester of the carbazole acid, and this would be insoluble in NaOH. The usual method of separation by basic extraction would be possible, and hydrolysis of the ester would readily yield the free carbazole acid.

Method (2) was chosen and found to be highly satisfactory.

Preparation of the ethyl ester of 6-carboxy-1:2:3:4-tetrahydrocarbazole.

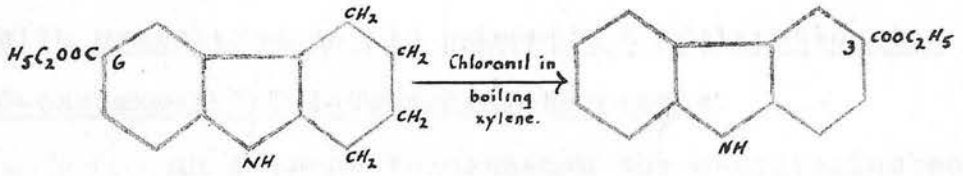
6-carboxy-1:2:3:4-tetrahydrocarbazole (4 gm.) was esterified by refluxing for 4½ hours with 40 c.c. ethyl alcohol, and 2 c.c. conc. sulphuric acid. The ester was precipitated by neutralising with dilute aqueous ammonia ; it was recrystallised /

recrystallised once from aqueous ethyl alcohol, then extracted with light petroleum (80-100°C.), hot filtered from a small amount of tarry residue, and allowed to crystallise from the light petroleum.

m.p. 114-116°C.

lit. m.p. 119°C. Yield = 2.3 gm.(50%).

Action of Chloranil on the ethyl ester of 6-carboxy-1:2:3:4-tetrahydrocarbazole.



The reflux period was 18 hours, after which a quantitative yield of tetrachlorohydroquinone was recovered, and the ethyl ester of carbazole-3-carboxylic acid obtained in good yield. After one crystallisation from a mixture of benzene and light petroleum, it crystallised in fine needle-prisms.

m.p. 156-158°C. lit. m.p. 165°C.

Hydrolysis of the ethyl ester of carbazole-3-carboxylic acid: hydrolysis was achieved by refluxing the ester (0.35 gm.) for 2 hours with 10 c.c. of 8% NaOH and 10 c.c. ethyl alcohol. The solution was diluted with water, and acidified with dilute hydrochloric acid, yielding 0.3 gm.(100%) of a white precipitate of the acid. m.p. 266°C. Colourless plates from glacial acetic acid m.p. 272-274°C. lit.m.p. 276-278°C.

Colour test: with conc.H_2SO_4 + 1 drop conc.HNO_3: carbazole 3-carboxylic acid and its ethyl ester both give an intense blue-green colour.

XV Preparation of carbazole-1-carboxylic acid.

1st stage: preparation of o-carboxyphenylhydrazine.
(o-hydrazinobenzoic acid).

The o-hydrazinobenzoic acid was prepared exactly as the para-acid. It crystallised in colourless needles and plates (hot water) m.p.240-244°C.
lit. m.p. 249°C.

2nd stage: condensation of o-hydrazinobenzoic acid with cyclohexanone and subsequent cyclisation to 8-carboxy-1:2:3:4-tetrahydrocarbazole.

An attempt to condense the o-hydrazinobenzoic acid with cyclohexanone by gently heating the reactants together, showed that in this case condensation would not readily occur by this method, and the following method was found to be very successful :-

The acid (1gm.) was dissolved in 50 c.c. hot water, and to the hot solution cyclohexanone (0.65 gm.) was added ; at once, the mixture became milky and, on shaking, deposited a yellow precipitate of fine needles in good yield. m.p. 154-156°C. It crystallised from benzene in very fine, pale yellow needles. m.p. 159-160°C with decomposition.
lit. m.p. 162°C.

4 gm. of cyclohexanone o-carboxyphenyl-hydrazone (obtained in the same way) were warmed gently with 20 c.c.conc. sulphuric acid and 80 c.c.water. The hydrazone dissolved, and on warming /

warming gently and shaking the solution for a very short time, 2.9 gm. of crude tetrahydro-compound were obtained. The 8-carboxy-1:2:3:4-tetrahydro - carbazole crystallised from benzene in small prisms .

m.p. 200-202°C. lit. m.p. 203°C.

Yield = 2 gm.(pure) : 55%.

Preparation of the ethyl ester of 8-carboxy-1:2:3:4-tetrahydrocarbazole.

The tetrahydrocarbazole (2 gm.) was refluxed with 20 c.c. alcohol and 1 c.c. conc. sulphuric acid for 5 hours; the ester was precipitated by the addition of very dilute aqueous ammonia, giving long, clean white needles m.p.72-74°C. On crystallisation from dilute alcohol, m.p. 74-75°C.

lit. m.p.76°C. Yield = 1.4 gm.(62%)

Action of Chloranil on the ethyl ester of 8-carboxy-1:2:3:4-tetrahydrocarbazole.

The ester (1 gm.) was refluxed for 24 hours with chloranil (2.02 gm.) in 15 c.c. sulphur-free xylene. Tetrachlorohydroquinone was recovered in quantitative yield, and the ethyl ester of carbazole-1-carboxylic acid obtained in clusters of colourless needles in 75% yield. After one crystallisation from methyl alcohol (charcoal), it was obtained as colourless needles and prisms.

m.p. 106-107°C.

lit. m.p. 106°C.

Analysis fd. C = 74.8% ; H = 5.30%.

$C_{15}H_{13}NO_2$ requires C = 75.3% ; H = 5.48 %.

Hydrolysis of the ester of carbazole-1-carboxylic acid.

Hydrolysis was carried out exactly as described for the hydrolysis of the ethyl ester of carbazole-3-carboxylic acid, again resulting in a 100% yield of the free acid. m.p.(crude) 264°C. The acid was recrystallised from glacial acetic acid (charcoal), yielding small colourless prisms.

m.p. 268-270°C.

lit. m.p. 270-271°C.

Colour test: with conc. H_2SO_4 + 1 drop conc. HNO_3: carbazole-1-carboxylic acid gives an intense blue-green colour.

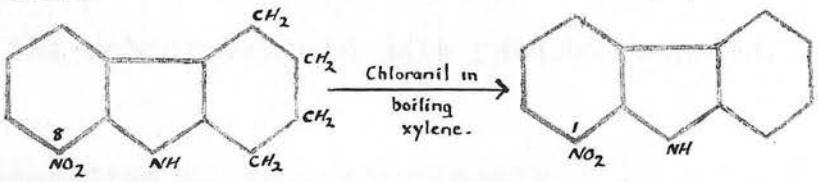
XV Preparation of 1-nitrocarbazole :

O-nitrophenylhydrazine was prepared by the method of Davies (J.C.S.,1922, 121, 717) already mentioned (see p.12) - reduction of o-nitrobenzene-diazonium chloride by sodium sulphite solution. The yield, however,was only 25%, due to the production of an insoluble by-product, formed possibly by incomplete reduction of the diazonium salt to the hydrazine. The crude o-nitrophenylhydrazine melted at 82°C., but a small sample which crystallised from benzene in deep-red needles, melted at 90°C.(lit.). Orange-brown plates (m.p.74°C. - lit.) of cyclohexanone o-nitrophenylhydrazone were readily obtained by condensing the o-nitrophenylhydrazine with cyclohexanone in alcoholic solution. The

hydrazone/

hydrazone dissolved in dilute sulphuric acid (1:9) and after refluxing the solution for about 1½ hours, crystals began to separate from the milky, brown solution , and on cooling thoroughly, an orange-brown precipitate of 8-nitro-1:2:3:4-tetrahydrocarbazole was obtained, which crystallised in yellow-brown plates from glacial acetic acid, m.p. 146-148°C. lit. m.p. 148-149°C.

Action of Chloranil on 8-nitro-1:2:3:4-tetrahydrocarbazole.



8-nitro-1:2:3:4-tetrahydrocarbazole (0.47 gm.) was refluxed for 6½ hours with chloranil (1.08 gm.) in 13 c.c. sulphur-free xylene. From the mixture, on cooling, a 50% yield of 1-nitrocarbazole was obtained along with a corresponding amount of tetrachlorohydroquinone. The xylene filtrate, after basic extraction which removed unchanged chloranil as the sodium salt of chloranilic acid, gave crystals, which after crystallisation from glacial acetic acid (charcoal), melted at 145-148°C., and were therefore unchanged 8-nitrotetrahydrocarbazole.

The 1-nitrocarbazole, obtained in 50% yield by the oxidation with chloranil, crystallised from alcohol in yellow-brown needles m.p. 185-187°C.

lit. m.p. 187°C.

The yield of 50% would undoubtedly be increased to at least 80% by allowing a longer period of reflux with chloranil as is shown by the result of experiment XVI (see p. 52) in which an 85 % yield of 3-nitrocarbazole was obtained after a 24-hour reflux of 6-nitro-1:2:3:4-tetrahydrocarbazole with chloranil.

Colour test : with conc. H_2SO_4, 1-nitrocarbazole gives a blue-black colour, changing quickly to greenish-brown, and on addition of a drop of conc. HNO_3 the colour becomes pale yellowish-green.

XVI Preparation of 3-nitrocarbazole.

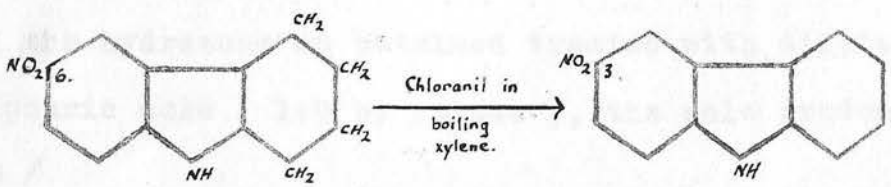
P-nitrophenylhydrazine (B.D.H.) readily condensed in alcoholic solution with cyclohexanone to give cyclohexanone p-nitrophenylhydrazone in good yield . Yellow needles m.p. 145-147°C.

lit. m.p. 146-147°C.

The hydrazone was refluxed for about three hours on the water-bath with dilute sulphuric acid (1:9 by volume) yielding 6-nitro-1:2:3:4-tetrahydro-carbazole, which, after two crystallisations from alcohol (charcoal) gave orange-brown prisms.

m.p.174°C. (lit.).

Action of Chloranil on 6-nitro-1:2:3:4-tetrahydro-carbazole.



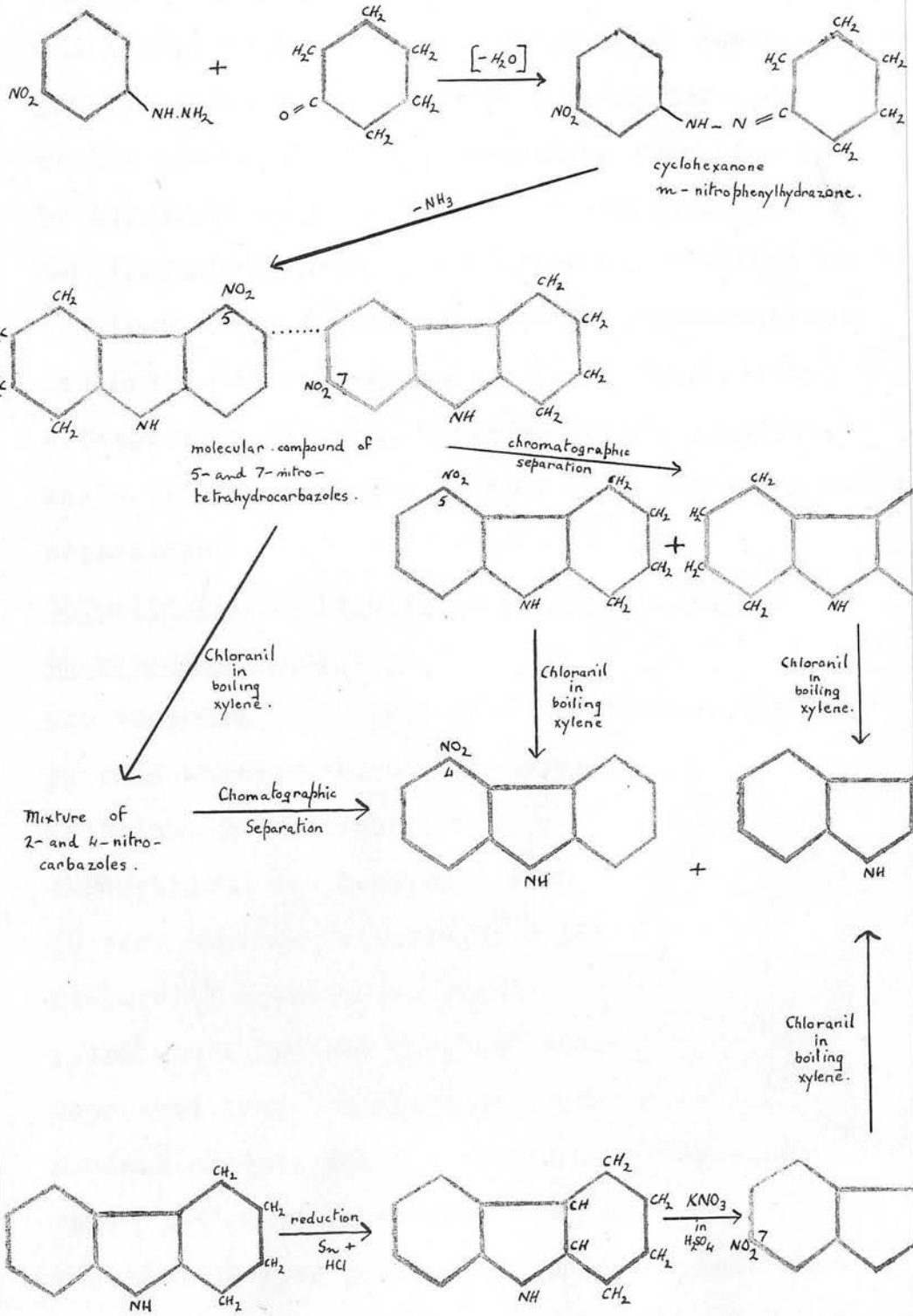
The period of reflux was 24 hours , after which time 80% of the tetrachlorohydroquinone was recovered, and 85% of crude 3-nitrocarbazole isolated. The latter, after one crystallisation from xylene, melted at 203-206°C. (lit.m.p. 213°C.). It was confirmed by mixed m.p. with a specimen of 3-nitrocarbazole already prepared by nitration of carbazole in glacial acetic acid (Ziersch, Ber., 1909, 42, 3797). No depression was observed.

Colour test : with conc.H_2SO_4 + 1 drop conc. HNO_3 : 3-nitrocarbazole gives a brilliant red colour with sulphuric acid, and on addition of 1 drop of nitric acid, the red changes to the typical intense blue-green colour shown by carbazole and its derivatives.

XVII Preparation of 2-nitrocarbazole and 4-nitrocarbazole.

As has already been explained (see p.20), the cyclisation of meta-substituted phenylhydrazones of cyclohexanone may be expected to yield a mixture of 5- and 7- substituted tetrahydrocarbazoles . By treatment of cyclohexanone m-nitrophenylhydrazone, it was hoped to prepare a mixture of 5- and 7- nitro-1:2:3:4-tetrahydrocarbazoles . However, when m-nitrophenylhydrazine hydrochloride was condensed with cyclohexanone in presence of sodium acetate, and the hydrazone so obtained treated with dilute sulphuric acid (1:9 by volume), the sole product was /

Summary of Experiments XVII to XIX.



was a compound which crystallised from methyl alcohol in compact prisms, m.p. 154-155°C. No amount of crystallisation raised the m.p. further, and the product was always obtained as compact prisms. (Plant, J.1936, 899 , gives the m.p. as 151-152°C.). It was therefore suspected that by sulphuric acid treatment of cyclohexanone m-nitrophenylhydrazone , a molecular compound of 5-nitrotetrahydrocarbazole and 7-nitrotetrahydrocarbazole had been formed : it was decided to attempt to " break up " the molecular compound, and so isolate the two isomers , by chromatographic separation.

Chromatographic Separation of 5- and 7-nitrotetrahydrocarbazoles.

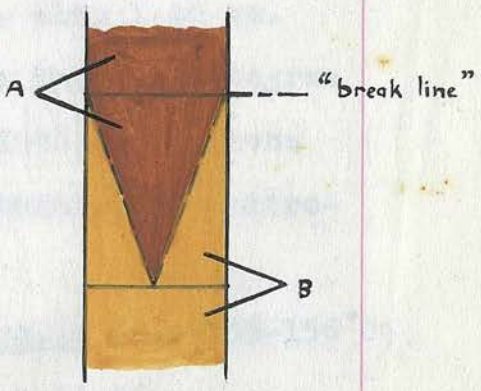
The compound (3.2 gm.) was dissolved in 300 c.c. of cold benzene and chromatographed (alumina, 30 × ½ inch). The chromatogram was developed with 50 c.c. benzene followed by a 3:1 mixture of benzene and light petroleum (100-120°C.), and soon separated into two distinct bands,

A- dark orange, and B - bright orange-yellow. Band " B " was washed down the column, and fourteen 50 c.c. portions of yellow eluate were collected, by which time most of band " B " had been washed through. Each portion of eluate was evaporated /

evaporated to about 5 c.c. and allowed to crystallise, yielding orange-red elongated prisms. m.p. 155-156°C. Mixed m.p. with the original molecular compound (154-155°C) : 142-143°C mainly , but a few remaining crystals melt up to 150°C. The yield of nitrotetrahydrocarbazole obtained from these fourteen portions of eluate was 1.2 gm. This must be 5-nitrotetrahydrocarbazole as 7-nitrotetrahydrocarbazole melts at 172°C. (Plant , J.1936, 899).

Band " A " and the remainder of band " B " were cut and extracted with alcohol . From " B ", by evaporation of the alcoholic extract, was obtained 0.08 gm. of crystals which, after one crystallisation from light petroleum (100-120°C.) melted at 152-153°C., and did not depress a sample of the above 1.2 gm., and was therefore also 5-nitrotetrahydrocarbazole.

Band " A " was quite uniform down to the "break line ", after which came a 3" band with " B " on the outside and " A " in a tubular channel as shown in the diagram alongside.



This section of the column was therefore cut at the " break line " and the upper portion extracted several times with ethyl alcohol, the combined extracts evaporated to about 50 c.c. then 50 c.c. warm water added, and the mixture cooled thoroughly, yielding /

yielding 1.19 gm. of yellow crystals. m.p. 168-172°C. The 3" " mixed band " (containing both A and B) was extracted several times with ethyl alcohol, evaporated, and 0.33 gm. crystals m.p. 159-162°C. precipitated by warm water . This precipitate was rechromatographed (alumina, 4x½ inch) and readily separated into 2 bands, A_1 and B_1. A_1, after extraction and precipitation as described above , yielded the higher-melting yellow isomer - 0.21 gm. The total yield of this isomer, 7-nitro-1:2:3:4-tetrahydrocarbazole, was therefore 1.40 gm., and the m.p. on recrystallisation (alcohol) was 171-172°C.

B_1, on similar treatment , yielded 0.12 gm. of orange crystals m.p. 155-156°C (light petroleum, 100-120°C.). The total yield of 5-nitro-1:2:3:4-tetrahydrocarbazole was,therefore, also 1.40 gm. Consequently, an 88% recovery from the chromatogram has been attained . Plant (J.1936, 899) gives the ratio of 5-nitrotetrahydrocarbazole to 7-nitro-tetrahydrocarbazole as 2:1 .

Analysis of 5-nitrotetrahydrocarbazole (m.p.155-156°C).

fd. C = 66.33%; H = 5.75% ; N = 13.4% .

$C_{12}H_{12}O_2N_2$ requires C = 66.63%; H = 5.6%; N = 13.0%.

(a) Action of Chloranil on 7-nitro-1:2:3:4-tetrahydrocarbazole. (m.p. 170-172°C.).

7-nitro-1:2:3:4-tetrahydrocarbazole (0.48 gm.) was refluxed for 18 hours with chloranil (1.09 gm.) in 14 c.c. sulphur-free xylene . After the usual treatment at the end of the reflux period, a 75% recovery of tetrachlorohydroquinone was attained and at least 60% of 2-nitrocarbazole was isolated . After two recrystallisations from benzene (charcoal), it crystallised as bright yellow glistening plates and prisms. m.p. 165-166°C. A mixed m.p. with 7-nitrotetrahydrocarbazole (172°C.) showed a depression of at least 20°C., therefore the product of oxidation is indeed 2-nitrocarbazole.

Analysis of 2-nitrocarbazole :

fd. (1) C = 66.7% ; H = 3.79% ; N = 13.1% .

fd. (2) after a further recrystallisation :

C = 67.0% ; H = 4.16% .

$C_{12}H_8O_2N_2$ requires C = 67.9% ; H = 3.8% ; N = 13.2% .

Colour test : with conc.H_2SO_4 + 1 drop conc. HNO_3 : 2-nitrocarbazole gives an intense blue-green colour.

(b) Action of Chloranil on 5-nitro-1:2:3:4-tetrahydrocarbazole. (m.p.155-156°C.).

5-nitro-1:2:3:4-tetrahydrocarbazole (0.47 gm.) was refluxed for 24 hours with chloranil (1.08 gm.) in 13 c.c. sulphur-free xylene. By the usual treatment /

treatment, 80% of the tetrachlorohydroquinone was recovered and 65% of 4-nitrocarbazole isolated (m.p.175-176°C.). On recrystallisation from benzene (charcoal-twice) , 4-nitrocarbazole crystallised as orange prisms , m.p.179-180°C ; mixed m.p. with 5-nitrotetrahydrocarbazole (155-156°C.) gave a considerable depression , showing that 4-nitrocarbazole had indeed been obtained by the oxidation .

Analysis of 4-nitrocarbazole:(m.p.179-180°C.):

fd. (1) C = 66.7% ; H = 3.71% ; N = 12.9% .

fd. (2) after a further recrystallisation:

C = 67.4% ; H = 4.12% .

$C_{12}H_8O_2N_2$ requires C = 67.9% ; H = 3.8% ; N = 13.2% .

Colour test: with conc.H_2SO_4 + 1 drop conc.HNO_3 : 4-nitrocarbazole gives an intense blue-green colour.

XVIII Alternative Preparation of 2-nitrocarbazole.

Nitration of hexahydrocarbazole by the method of Gurney, Perkin and Plant (J.1927,130,1320) produces 7-nitrohexahydrocarbazole. It was decided to prepare this compound and oxidise it with chloranil in boiling xylene to 2-nitrocarbazole.

Preparation of 7-nitrohexahydrocarbazole:

10 gm. of hexahydrocarbazole (prepared as already described - see p. 35) were dissolved in 100 c.c. concentrated sulphuric acid and treated gradually with 5.8 gm. of powdered potassium nitrate, maintaining /

maintaining the temperature at°3 C. The mixture was allowed to stand for 15 minutes, poured onto ice, and made alkaline with concentrated ammonia (maintaining at 0°C. by the addition of ice). An oily product was thus obtained , which after a time solidified . It was purified by repeated extraction with ethyl alcohol, followed by the addition of warm water to the combined extracts until a slightly turbid warm solution was obtained . On cooling the solution, 7 gm. of yellow needles of 7-nitrohexahydrocarbazole were obtained. m.p. 69°C.(lit.).

Action of Chloranil on 7-nitrohexahydrocarbazole.

1 Molecular proportion of 7-nitrohexahydrocarbazole was refluxed for 19 hours in xylene with 3 molecular proportions of chloranil . 85% of the tetrachlorohydroquinone was recovered and a 75% yield of crude 2-nitrocarbazole, m.p.156-159°C. isolated . After two recrystallisations from benzene, it melted at 164-166°C., and gave no depression with a sample of 2-nitrocarbazole obtained by oxidation of 7-nitro-1:2:3:4-tetrahydrocarbazole (experiment XVII - see p. 56) .

Analysis : fd. C = 66.1% ; H = 3.53% .

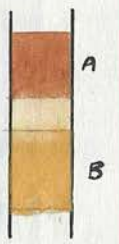
$C_{12}H_8O_2N_2$ requires C = 67.9% ; H = 3.8% . (cf.p. 56).

In this oxidation a very small amount (about 2%) of a very insoluble, high-melting by-product was isolated; as in other cases, it was not further investigated.

XIX Alternative Preparation of 2- and 4-nitrocarbazole.

Oxidation of the molecular compound (m.p.154-155°C.) of 5- and 7-nitro-1:2:3:4-tetrahydrocarbazoles with chloranil in boiling xylene should yield a product consisting of a mixture of 2- and 4-nitrocarbazoles, which should be separable by chromatographic adsorption in the same way as the 5- and 7-nitrotetrahydrocarbazoles. It was decided to attempt to prepare 2- and 4-nitrocarbazoles by this method, and compare them with the products obtained in experiment XVII.

The molecular compound of 5- and 7-nitrotetrahydrocarbazoles (2.31 gm.) was refluxed for 25 hours with chloranil (5.25 gm.) in 50 c.c. sulphur-free xylene. By the usual treatment , a 90% recovery of tetrachlorohydroquinone was achieved, and a 60% yield of a very clean, orange oxidation product , m.p.132-133°C , was obtained. 1.14 gm. of this product were dissolved in 100 c.c. cold benzene and chromatographed (alumina, 15x½ inch.). The chromatogram was developed by washing first with benzene then with a 3:1 mixture of benzene and light petroleum (100-120°C.), giving a good separation of two distinct bands, "A" - dark orange, and "B" - light orange-yellow, as shown in the diagram above.



After 300 c.c. elution agent had been added , most of /

of band "B" had washed through, so the chromatogram was drained and cut.

(1). The eluate containing most of "B" on evaporation gave 0.31 gm. orange crystals, which, after two recrystallisations from benzene, melted at 179-180°C., and showed no depression with 4-nitrocarbazole obtained by chloranil oxidation of 5-nitro-1:2:3:4-tetrahydrocarbazole, and was, therefore, also 4-nitrocarbazole.

Analysis : fd. C = 67.4% ; H = 4.13% .

$C_{12}H_8O_2N_2$ requires C = 67.9% ; H = 3.8 % . (see p.57).

(2). The remainder of "B" was obtained by extracting the remainder of band "B" with methyl alcohol, adding warm water to the warm alcoholic solution, and thoroughly cooling the mixture, yielding 0.02 gm. precipitate, m.p. 179-180°C. This was also 4-nitrocarbazole .

(3). The portion of the column between the bands "A" and "B" was also extracted with alcohol, and 0.21 gm. of yellow-orange precipitate, m.p.150-170°C., was precipitated with water. It was assumed that this fraction was still a mixture of the two isomers, but it was not re-chromatographed.

(4). Band "A" was extracted with methyl alcohol, the combined extracts evaporated to about 50 c.c. and 50 c.c. warm water added. On cooling the mixture, 0.49 gm. of precipitate was obtained. After three recrystallisations /

recrystallisations from benzene (charcoal) it melted at 165-166°C., and gave no depression with 2-nitrocarbazole obtained (a) by oxidation of 7-nitrohexahydrocarbazole (see p. 58), and (b) by oxidation of 7-nitrotetrahydrocarbazole (see p.56). Band "A" therefore contained 2-nitrocarbazole .

Analysis : fd. C = 66.0% ; H = 4.16% .

$C_{12}H_8O_2N_2$ requires C = 67.9% ; H = 3.8% .

Repeat analysis after a further crystallisation from alcohol :

fd. C = 66.1% ; H = 3.53% .

Recovery of isomers : 0.33 gm. of 4-nitrocarbazole.

0.49 gm. of 2-nitrocarbazole.

+ 0.21 gm., m.p. 150-170°C., (a mixture of 2- and 4- nitrocarbazoles, but probably mainly 4-nitrocarbazole).

Total recovery = 1.03 gm. (90%).

Two small-scale experiments carried out in this laboratory (by Dr. Campbell) support the evidence obtained in the previous experiments XVII to XIX. (1). 4 mg. of 5-nitro-1:2:3:4-tetrahydrocarbazole, m.p.155-156°C. (from chromatograph) + 4 mg. 7-nitro-1:2:3:4-tetrahydrocarbazole, m.p.171-172°C. (from chromatograph) were dissolved in the minimum of hot alcohol. On cooling the solution, 6 mg. of crystals, m.p. 154-156°C. were obtained . No depression of m.p. was obtained with the original compound /

compound prepared by cyclisation of cyclohexanone m-nitrophenylhydrazone , but a depression was given with each isomer —— 5-nitro and 7-nitro-tetrahydrocarbazole . Therefore , in cyclisation of cyclohexanone m-nitrophenylhydrazone , a molecular compound is formed.

(2) On nitration of N-acetyltetrahydrocarbazole, 7-nitro-N-acetyltetrahydrocarbazole is obtained (Plant, J.1936, 899). On hydrolysis with NaOH in 50% alcohol, 7-nitro-1:2:3:4-tetrahydrocarbazole was obtained. It gave no depression with 7-nitro-1:2:3:4-tetrahydrocarbazole obtained from the chromatographic separation (see p.53).

Colour Tests of Nitrocarbazoles.

Compound	conc.H_2SO_4.	+ 1 drop conc.HNO_3
1-nitrocarbazole.	blue-black to greenish-brown	pale yellow-green
2-nitrocarbazole (from hexahydro-carbazole.)	nil	intense blue-green
2-nitrocarbazole (from tetrahydro-carbazole).	nil	intense blue-green
3-nitrocarbazole.	brilliant red	intense blue-green
4-nitrocarbazole.	nil	intense blue-green

1- , 2- , 3- , and 4-nitrocarbazoles give a bright red colour with methyl alcoholic KOH.

Note : The xylene solutions containing the various products of oxidation of the substituted tetrahydrocarbazoles with chloranil varied in colour from light amber to purple, and without exception showed a strong fluorescence (generally purple) in Ultra-violet light . The intensity of the fluorescence appeared to be increased when the xylene solutions were washed with 4% KOH solution to remove tetrachlorohydroquinone formed in the oxidation.

9-Substituted-Tetrahydrocarbazoles.

At one stage in the course of the research, it was decided to investigate the action of chloranil on 9-substituted-tetrahydrocarbazoles, as it was felt that the oxidation of substituted tetrahydrocarbazoles might proceed even more smoothly, if the 9- position was also substituted. For example, the possibility of 9:9' dicarbazyl formation would be precluded . With this aim in view , several attempts were made to prepare 9-substituted-tetrahydrocarbazoles , without much success .

(1) When an attempt was made to acetylate tetrahydrocarbazole by dissolving tetrahydrocarbazole in acetone and 66% aqueous KOH , and treating the solution with acetyl chloride (method of Stevens and Tucker, J.1923, 123, 2140 , for preparation of N-derivatives of carbazole /

carbazole and 3-nitrocarbazole), tetrahydrocarbazole was recovered unchanged, as shown by m.p., and mixed m.p. with an authentic sample.

(2) An attempted preparation of N-benzoyltetrahydrocarbazole by the same method was also unsuccessful.

(3) Two attempts to prepare N-methyltetrahydrocarbazole by the same method (J.1923, 123, 2147) resulted in unchanged tetrahydrocarbazole.

(4) An attempt to acetylate tetrahydrocarbazole by refluxing for one hour with acetic anhydride (method used by Moggridge and Plant, J.1937,1127 for acetylation of 7-chloro-1:2:3:4-tetrahydrocarbazole) again resulted in unchanged tetrahydrocarbazole.

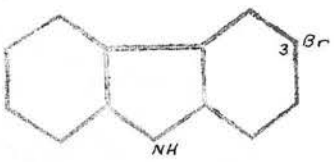
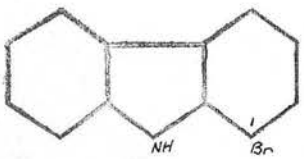
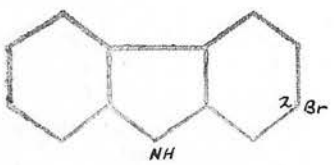
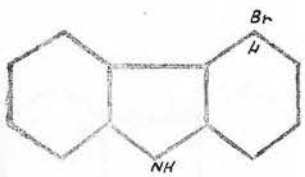
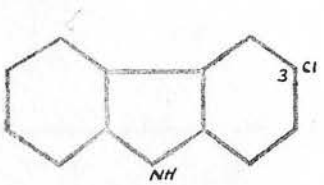
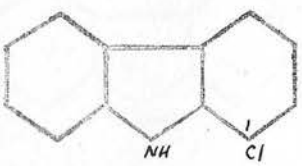
A further attempt at acetylation using a mixture of acetic anhydride and acetyl chloride did actually produce colourless prisms m.p. 73-74°C.(alcohol). This was assumed to be 9-acetyl-1:2:3:4-tetrahydrocarbazole (lit.m.p. 77°C.). The result of refluxing this compound with chloranil for 6 hours in boiling xylene was not at all satisfactory, as a very complex mixture resulted, from which tetrachlorohydroquinone was only recovered with difficulty , along with some unchanged chloranil, and a high-melting very insoluble product which gives a dark blue-green colour with conc.H_2SO_4 + conc.HNO_3.

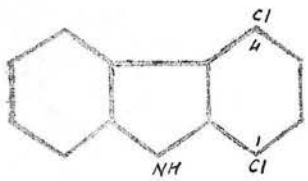
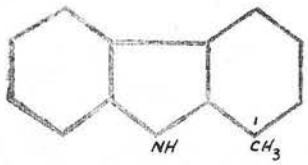
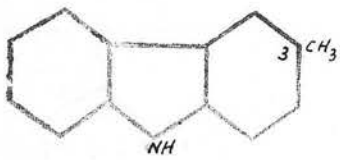
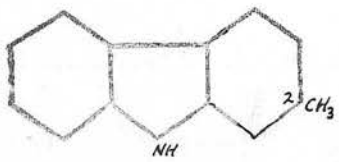
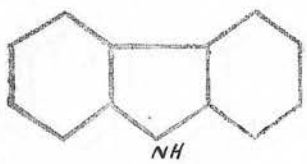
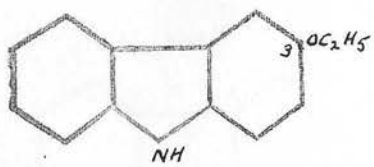
(5) It was decided then to attempt to repeat the preparation of N-benzoylcarbazole by the method of Dunlop /

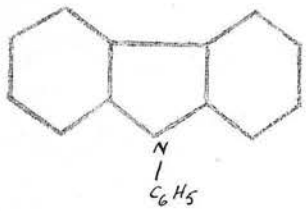
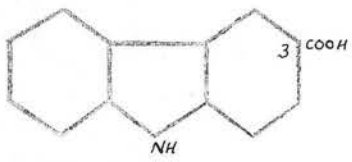
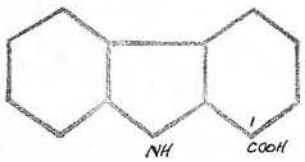
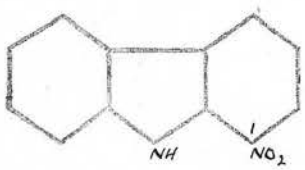
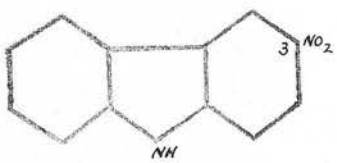
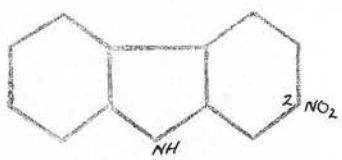
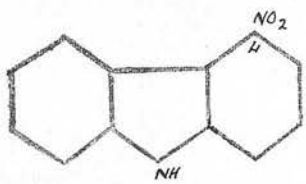
Dunlop and Tucker (J.C.S. 1939, 1956). Unchanged carbazole was obtained by this method , perhaps due to the fact that in the experimental instructions no mention is made of copper bronze, whereas the presence of a trace of copper bronze is recommended in the introductory discussion (same reference, p.1948).

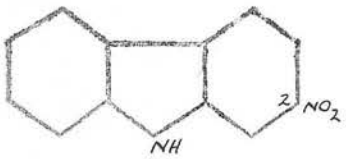
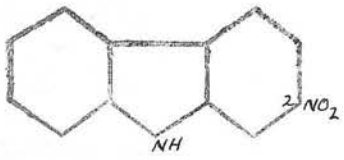
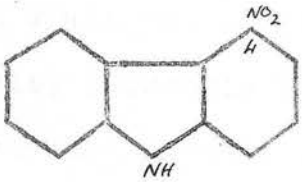
The only N-substituted-tetrahydrocarbazole prepared successfully was N-phenyltetrahydrocarbazole, which was very satisfactorily oxidised to N-phenylcarbazole by chloranil in boiling xylene (see experiment XII , p. 41). The N-phenyltetrahydrocarbazole was not prepared, however, by arylation of tetrahydrocarbazole , but by reduction of nitrosodiphenylamine with zinc dust and acetic acid in presence of cyclohexanone.

TABLE OF EXPERIMENTAL RESULTS.

Compound.	Experiment and Page No.	Yield by chloranil oxidation of corresponding tetrahydrocarbazole.
	Expt. I p. 12.	71% yield - 18 hour reflux. m.p. 198-9°C. lit. m.p. 199°C.
	Expt. II p. 17.	87% yield - 21.5 hour reflux. m.p. 111-2°C.
	Expt. III p. 20.	85% yield - 24 hour reflux. m.p. 250-1°C.
	Expt. III p. 20.	81% yield of mixture of 2-and 4-bromocarbazoles 56% yield of 4-bromocarbazole by chromatographic separation . m.p. 104-5°C.
	Expt. IV p. 25.	50% yield - 24 hour reflux. m.p. 199-200°C. lit.m.p. 201.5°C.
	Expt. V p. 26.	90% yield - 24 hour reflux. m.p. 109-110°C. lit. m.p. 125°C.

	Expt. VI p. 28.	75% yield - 11 hour reflux. m.p. 90-92°C.
	Expt. VII p. 30.	70% yield - 18 hour reflux. m.p. 114°C. lit.m.p. 120.5°C.
	Expt. VIII p.31.	50% yield - 18 hour reflux . m.p. 199-202°C. lit. m.p. 203°C.
	Expt. IX p. 33.	Good yield - 18 hour reflux. m.p. 259°C.(lit.).
	Expt. X p. 34.	(a). Quantitative yield from tetrahydrocarbazole - 24 hour reflux. (b). 70% yield from hexahydrocarbazole - 1 hour reflux. (c). 83% yield from dihydrocarbazole - 24 hour reflux. m.p. 244-246°C. lit. m.p. 246°C.
	Expt. XI p. 38.	90% yield - 1 hour reflux. m.p.105-106°C. lit.m.p. 106-107°C.

	Expt. XII p. 41.	96% yield - 24 hour reflux. m.p.87-89°C. lit. m.p.94-95°C.
	Expt. XIII p. 42.	Good yield of ethyl ester of acid - 24 hour reflux. Hydrolysis to acid- 100%. m.p. 272-274°C. lit.m.p.276-278°C.
	Expt. XIV p. 46. 7	75% yield of ethyl ester of acid - 24 hour reflux. Hydrolysis to acid - 100%. m.p. 268-270°C. lit.m.p.270-271°C.
	Expt. XV p. 49.	50% yield after 6.5 hour reflux. m.p. 186 -187°C. lit.m.p. 187°C.
	Expt. XVI p. 51.	85% yield - 24 hour reflux. m.p. 203-206°C. lit. m.p. 213°C.
	Expt. XVII p. 52.	At least 60% yield- 18 hour reflux. m.p. 165-166°C.
	Expt. XVII p.52.	65% yield - 24 hour reflux. m.p. 179-180°C.

	Expt. XVIII p. 57.	75% yield - 19 hour reflux. m.p. 164-166°C.
 	Expt. XIX p. 59.	At least 60% yield of oxidation product, m.p.132-3°C. (mixture of 2- and 4-nitrocarbazoles. 90% recovery in chromatographic separation, and 50-50 yield of each isomer obtained. 2-nitrocarbazole- m.p.165-166°C. 4-nitrocarbazole- m.p.179-180°C.

DISCUSSION OF EXPERIMENTAL RESULTS.

By the low temperature dehydrogenation of substituted tetrahydrocarbazoles with chloranil in boiling xylene, many mono-substituted carbazoles of different types have been prepared in good yield - some of them for the first time. The various oxidising agents previously employed have been found suitable in certain cases, but no reagent had been found which was of general applicability . For example, Borsche's method of passing the substituted tetrahydrocarbazole over lead oxide (Ann.1908, 359,49) was successful in the case of methyl-tetrahydro-carbazoles, but was useless for halogen- or nitro-derivatives . Similarly, although dehydrogenation with sulphur and quinoline can be applied to halogen-compounds, it is not suitable for nitro- or carboxy-compounds - when Perkin and Plant (J.1923, 123, 676) tried to obtain 3-nitrocarbazole by sulphur dehydrogenation of 6-nitro-1:2:3:4-tetrahydrocarbazole they obtained a black resin, and $COOC_2H_5$ was removed from 9-carbethoxy-tetrahydrocarbazole resulting in carbazole itself in 23% yield . The only advantage of the sulphur-quinoline oxidation, in cases where it is applicable, is the short time required - generally about ½ hour ; as can be seen from the experimental section , most dehydrogenations with chloranil in boiling xylene require about 24 hours reflux, although there are exceptions. However, this small

disadvantage /

disadvantage is completely outweighed by the fact that chloranil is of general applicability , as has been shown by the preparation of halogeno-, nitro-, methyl-, ethoxy-, and N-substituted derivatives, and in yields which are much higher than have previously been obtained by any other oxidation method. Moreover, the comparatively low temperature at which the dehydrogenation is carried out is decidedly advantageous, as it is known, for example, that at the high temperatures necessary for selenium dehydrogenations, thermal arrangements tend to occur. From the commercial point of view, the chloranil dehydrogenation process is very satisfactory, since the tetrachloro-hydroquinone is always recovered in good yield and can be reconverted quantitatively to chloranil by oxidation with nitric acid. (Arnold, Collins, and Zenk, J.A.C.S.1940, 62, 983.).

Most of the discussion arising from the experimental section concerns the dehydrogenation process, but as other points arise in the case of the preparation of certain derivatives, each experiment will now be dealt with in turn, and it is hoped by this means to show the superiority of the chloranil method over other dehydrogenation methods for the preparation of substituted carbazoles from the corresponding tetrahydrocarbazoles.

Experiment 1 , p. 12. Preparation of 3-bromocarbazole.

There are two standard methods for the preparation of 3-bromocarbazole /

3-bromocarbazole - (a) by saponification of 9-acetyl-3-bromocarbazole, which in turn is prepared from bromination of 9-acetylcarbazole, and (b) treatment of carbazole-3-diazonium bromide with copper . The yields are not good however, and in particular by method (b), the yield is small as carbazole itself is also produced. However, by chloranil oxidation of 6-bromo-1:2:3:4-tetrahydrocarbazole, at least a 70% yield of 3-bromocarbazole has been obtained .
(Perkin and Plant obtained a 20% yield by a sulphur dehydrogenation of 6-bromo-1:2:3:4-tetrahydrocarbazole - J.1923, 123, 676.). The tetrahydro-compound was readily prepared in very good yield by condensation of p-bromophenylhydrazine with cyclohexanone, although samples of B.D.H. p-bromophenylhydrazine hydrochloride which had been kept for some time were found to be useless for this purpose. Preparation of the p-bromophenylhydrazine required for this condensation at first presented some difficulty until the method of Bülow was tried. Bülow recommends the presence of a large excess of concentrated hydrochloric acid in the diazotisation of the corresponding halogeno-amine with sodium nitrite, to prevent formation of aminoazo by-products. The tin double salt of the halogeno-phenylhydrazine, obtained by reduction of the diazo-compound with stannous chloride solution, was, rather surprisingly, readily decomposed by 2N NaOH. By this method a very clean sample of bromophenyl-

hydrazine /

phenylhydrazine was obtained in good yield, and, as has been shown in the experimental section, the method was found to be equally suitable(with slight modification) for the preparation of carboxyphenylhydrazines and ethoxyphenylhydrazine.

The period of reflux necessary for complete dehydrogenation was found by testing a few drops of the reflux mixture at intervals for unchanged chloranil with sodium hydroxide . In the case of the halogeno-tetrahydrocarbazoles, the period of reflux was generally from 18 to 24 hours, after which time the tetrachlorohydroquinone was usually recovered in almost quantitative yield indicating that a good yield of oxidation product might reasonably be expected.

As has already been mentioned in the experimental section, a small amount of a high-melting very insoluble by-product was isolated in the oxidation of 6-bromo-1:2:3:4-tetrahydrocarbazole. This might correspond to 6:6'-dibromo-3:3'-dicarbazyl, as 3:3'-dicarbazyl is known to be high-melting and exceedingly insoluble in the usual organic solvents. (Tucker, J.1926, 3033). Moreover, 3:3'-dicarbazyl gives an inky-blue colour with conc.H_2SO_4 + 1 drop of conc.HNO_3 , as does the by-product isolated above. The very small quantity isolated did not merit further investigation during the course of the research. It is interesting to note, however, that

chloranil /

chloranil in boiling xylene did not affect carbazole itself in any way.

Experiment II, p.16. Preparation of 1-bromocarbazole.

The only reference to 1-bromocarbazole to be found was in Chemisches Zentral-Blatt,1931,2, 2215, where a patent is given for the preparation of 1-chloro, 1-bromo-, and 1-iodocarbazole by removal of $-SO_3H$ groups from 1-bromocarbazole-3:6:8-trisulphonic acid etc. No M.P. or yield is given for the 1-bromocarbazole. However, by oxidation of 8-bromo-1:2:3:4-tetrahydrocarbazole with chloranil in boiling xylene, an 87% yield of 1-bromocarbazole (m.p. 111-112°C.) has been achieved. The 8-bromotetrahydrocarbazole could not be induced to crystallise, and was always obtained as a heavy viscous oil.

Experiment III, p.20. Preparation of 2- and 4-bromocarbazoles. These two isomers, which complete the list of mono-bromocarbazoles, have not previously been prepared, although the corresponding tetrahydrocarbazoles are listed. (Plant and Wilson, J.1939, 237). Crystalline 7-bromo-1:2:3:4-tetrahydrocarbazole was readily obtained from the cyclisation of cyclohexanone m-bromophenylhydrazone, and gave an 85% yield of 2-bromocarbazole (m.p.250-251°C.) after a 24 hour reflux with chloranil in xylene. When the alcoholic filtrate after crystallisation of the 7-bromotetrahydrocarbazole was evaporated, the oily residue was expected to contain 5-bromo-1:2:3:4-tetrahydrocarbazole. However, /

However, when the oily residue was oxidised with chloranil, no sign of any isomer other than 2-bromocarbazole was evident. The whole process was repeated and care taken to remove as much 7-bromotetrahydrocarbazole as possible (assuming that a 1:1 ratio of 5- and 7-bromotetrahydrocarbazole was formed in the cyclisation). The oily residue so obtained was treated with chloranil giving a total yield of 81% oxidation product. 10% of this was 2-bromocarbazole which readily crystallised from the xylene, and the xylene filtrate on chromatographing yielded at least 56% of pure 4-bromocarbazole m.p. 104-105°C.

Experiment IV, p.25. Preparation of 3-chlorocarbazole.

Borsche's attempt to prepare 3-chlorocarbazole by leading the 6-chloro-1:2:3:4-tetrahydrocarbazole over lead oxide was unsuccessful, the halogen being eliminated and carbazole obtained. Chlorine is also removed when halogenotetrahydrocarbazoles are dehydrogenated with palladised charcoal in an atmosphere of hydrogen. (Moggridge and Plant, J. 1937, 1125.). So far, the best method of preparing 3-chlorocarbazole has been according to the general method (see p. 3) of Ullmann (Ann,1904, 332, 96) by distillation of the corresponding triazole, resulting in a good yield of the chlorocarbazole. By dehydrogenation of 6-chloro-1:2:3:4-tetrahydrocarbazole, readily prepared in good yield by the

usual /

usual condensation and cyclisation processes, with chloranil in xylene at least a 50% yield of pure 3-chlorocarbazole has now been obtained.

Experiment V , p.26. Preparation of 1-chlorocarbazole.

The only reference given in connection with 1-chlorocarbazole is that already noted (see p.74) in Chem.Zentr.1931, 2, 2215. The m.p. quoted for 1-chlorocarbazole is 125°C. By dehydrogenation of 8-chloro-1:2:3:4-tetrahydrocarbazole with chloranil in xylene a 90% yield of 1-chlorocarbazole was obtained. However, even after repeated recrystallisation from methyl alcohol, the m.p. could not be raised above 109-110°C.

Experiment VI, p.28. Preparation of 1:4-dichlorocarbazole.

This compound has not previously been listed. It was obtained in at least 75% yield by dehydrogenation of 5:8-dichloro-1:2:3:4-tetrahydrocarbazole . The difficult step in this synthesis was the cyclisation of the cyclohexanone 2:5-dichlorophenylhydrazone, and in the course of the research, several alternative cyclisation processes were attempted ; finally it was shown that the usual treatment with dilute sulphuric acid (1:9 by volume) was as satisfactory as any other reagent which was tried, although the tetrahydrocarbazole so obtained required considerable purification.

Experiment VII , p.30. Preparation of 1-methylcarbazole.

1-Methylcarbazole was prepared by Ullmann

by /

by distillation of the corresponding benztriazole carboxylic acid with quicklime. The yield, however, was not good. Dehydrogenation of 8-methyl-1:2:3:4-tetrahydrocarbazole with chloranil in xylene has now afforded a method of preparing 1-methylcarbazole in at least 70% yield. The 8-methyltetrahydrocarbazole, which had not previously been listed, was readily obtained by the usual condensation and cyclisation processes. The analysis of the picrate of the tetrahydro-compound produced a high result for nitrogen. This was not unexpected as the picrate was observed to decompose ; a higher proportion of picric acid might therefore have been present in the sample analysed.

Experiment VIII, p. 31. Preparation of 3-methylcarbazole.

3-methylcarbazole has previously been prepared by two dehydrogenation processes : (a) by distilling 6-methyl-1:2:3:4-tetrahydrocarbazole over lead oxide, Borsche(Ann.1908, 359, 77) obtained 3-methylcarbazole in about 50% yield; (b) Oakeshott and Plant (J.1926, 1212) dehydrogenated 6-methyl-tetrahydrocarbazole by sulphur in quinoline, but no yield of 3-methylcarbazole is quoted. Ullmann reported an 84% yield of the compound by distillation over quicklime of the corresponding benztriazole carboxylic acid. Dehydrogenation of 6-methyl-tetrahydrocarbazole with chloranil in boiling xylene has now resulted in at least a 50% yield of the 3-methylcarbazole.

Experiment IX, p.33. Preparation of 2-methylcarbazole.

Although two products were to be expected from condensation of m-methylcyclohexanone and phenylhydrazine , followed by cyclisation , only one product was isolated. It yielded 2-methylcarbazole in good yield by dehydrogenation with chloranil in boiling xylene. Borsche (Ann.1909, 359, 75) had obtained the compound in 40% yield by distilling the tetrahydro-compound over lead oxide. The analysis of the 2-methylcarbazole obtained by chloranil dehydrogenation was not very satisfactory (see p.34), but the m.p.'s of the compound and of its picrate agreed with those given in the literature.

Experiment X, p.34. Preparation of carbazole.

Carbazole has been prepared from tetrahydrocarbazole by several different dehydrogenation processes. Borsche obtained it by his usual method of leading the tetrahydro-compound over lead oxide, but he quotes no yield. Perkin and Plant (J.1921, 119, 1825) found that potassium permanganate would not oxidise tetrahydrocarbazole, but they did obtain carbazole (in very small yield) by treating tetrahydrocarbazole with mercuric oxide in glacial acetic acid at 85°C. for a few minutes. Later, the same authors (J.1923,123, 676) attained a 30% yield of carbazole by dehydrogenation with sulphur in quinoline. More recently (J.1939, 872), Gulland

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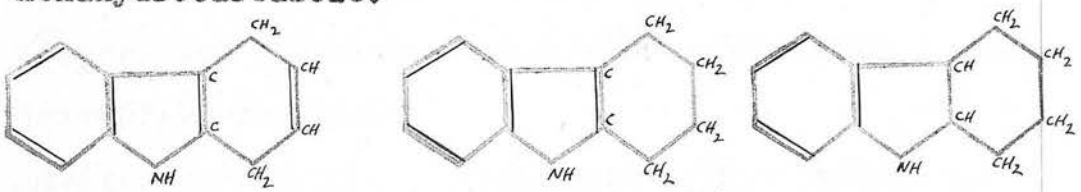
and Cooker, using a 2% aqueous solution of palladous chloride, recorded a 91% yield by dehydrogenation of tetrahydrocarbazole. Their yield, however, is calculated on the basis of the weight of palladium deposited and not on the amount of oxidation product isolated. Moreover, the method is obviously unsuitable for substances insoluble or sparingly soluble in water.

Carbazole has now been obtained by dehydrogenation by chloranil in boiling xylene of dihydrocarbazole, tetrahydrocarbazole, and hexahydrocarbazole.



In no case was the yield less than 70% of pure carbazole, and this was obtained from hexahydrocarbazole after only 1½ hours reflux with chloranil. This was somewhat unexpected as a 24 hour reflux was necessary for both dihydrocarbazole and tetrahydrocarbazole. It would seem to indicate that in the case of hexahydrocarbazole the reduced bond of the pyrrole part of the molecule is attacked immediately, and that once the oxidation has started, completion is attained very rapidly. This synthetic preparation of carbazole is, therefore, highly recommendable, as hexahydrocarbazole is readily obtained in good yield by reduction of tetrahydrocarbazole.

In the chromatographic purification of dihydrocarbazole, it /

it was rather surprising to find that only portions of eluate giving a blue-green colour with conc. H_2SO_4 + 1 drop of conc. HNO_3 yielded dihydrocarbazole on evaporation . Moreover, the intensity of the colour was such as to preclude the possibility of it being due solely to a trace of carbazole not separated from the dihydrocarbazole by chromatographing.

Although the nitrogen analysis of the trinitrobenzene compound of dihydrocarbazole was excellent, the hydrogen figure for dihydrocarbazole itself was disappointingly unsatisfactory. The following are the theoretical carbon and hydrogen figures for carbazole, dihydrocarbazole, and tetrahydrocarbazole :

Carbazole C = 86.19% ; H = 5.43% .

Dihydrocarbazole : C = 85.16% ; H = 6.64%.

Tetrahydrocarbazole : C = 84.16% ; H = 7.66%.

The result of the analysis of the dihydrocarbazole, purified by twice chromatographing, followed by twice recrystallising from glacial acetic acid , was : C = 84.9% ; H = 5.78% . The result for carbon agrees reasonably well with the theoretical figure for dihydrocarbazole . The hydrogen figure - the more important in such a case - would seem to indicate, however, that the dihydrocarbazole had not been completely freed from contaminating carbazole. On the other hand, the experimental facts, (1) that exactly one molecular proportion /

proportion of chloranil was sufficient to oxidise the dihydrocarbazole, and (2) that no unchanged chloranil was found after completion of the oxidation as would have been the case if there had been an appreciable amount of carbazole in the dihydrocarbazole , oppose the suggestion that the discrepancy in the hydrogen figure above is due to the presence of carbazole. Moreover, these facts rule out the possibility advanced by Schmidt and Schall (Ber.1907, 40, 3229) from consideration of their analysis figures for the compound — C= 85.41%; H = 5.96% — that it was a molecular compound of carbazole and dicarbazole. Finally, the picrate and trinitrobenzene compound prepared (see p.37) from the dihydrocarbazole are quite different from those of carbazole , and the discrepancy in the hydrogen figure for the dihydrocarbazole remains unexplained.

Experiment XL, p.38. Preparation of 3-ethoxycarbazole.

3-Ethoxycarbazole was only obtained in poor yield by Ruff and Stein (Ber.1901, 34, 1683) from 3-aminocarbazole. Hoshino and Takiura (Bull.Chem. Soc.Japan, 1936, 218) prepared it in 80% yield by dehydrogenation of 6-ethoxy-1:2:3:4-tetrahydrocarbazole using palladium black and cinnamic acid. The disadvantages of this method are that catalytic methods are sometimes capricious and the preparation of the catalyst is often a long and tedious process. Dehydrogenation by chloranil in boiling xylene has now /

has now yielded 3-ethoxycarbazole in 90% yield. In this case, only a short period of reflux (1 hour) was found to be necessary. In fact, with longer periods of reflux a very sticky product was obtained which was exceedingly difficult to purify. The experimental modifications made to Hoshino and Takiura's method of preparing the p-ethoxyphenylhydrazine have already been discussed (see pp.38-39).

Experiment XII, p.41. Preparation of 9-phenylcarbazole.

Hager (Organic Synthesis, Vol I, p.532, note 13) reports an 88% yield of 9-phenylcarbazole by treating carbazole with iodobenzene and anhydrous potassium carbonate. Tucker and Dunlop (J.1939, 1945) introduce a trace of copper bronze in the above method, but only report a 65% yield of the compound. 9-Phenylcarbazole has now been obtained in 95% yield by dehydrogenation of 9-phenyltetrahydrocarbazole with chloranil in boiling xylene . This was an exceedingly clean oxidation, the expected products being readily obtained at the end of the reflux period. Moreover, there was no trace of any high-melting insoluble by-product as had been noted in several other chloranil dehydrogenations ; this might indicate that some of the high - melting by-products might be substituted N:N'-dicarbazyls, although N:N'-dicarbazyl itself is quite a soluble compound with a reasonable m.p. (the possibility of substituted 3:3' dicarbazyls has already been discussed - see p. 73). This led to attempts to prepare /

prepare other 9-substituted -tetrahydrocarbazoles, and the unsatisfactory results obtained in this direction have already been fully discussed (see pp. 63-65).

Experiment XIII, p.42. Preparation of carbazole-3-carboxylic acid. Bulow's method for preparing halogeno-phenylhydrazines was found to be readily applicable to carboxy-phenylhydrazines with the slight modification of procedure mentioned in the experimental section (see p.42.). As has also been described, it has been proved that dehydrogenation with chloranil in xylene does not remove the -COOH group. However, for purposes of separation from tetrachlorohydroquinone, it is advantageous to carry out the dehydrogenation on an ester of the carboxy-tetrahydrocarbazole from which the free acid is readily obtained by hydrolysis . By this means pure carbazole-3-carboxylic acid has been prepared in good yield. Previously, Plant and Williams (J. 1934, 1142) prepared the acid by fusion of 3-acetyl-carbazole with KOH, but the purification involved formation of the ethyl ester followed by saponification to the acid. Moggridge and Plant (J.1937, 1125) reported the dehydrogenation of methyl-carbazole-6-carboxylate in good yield on heating for 5 hours at 280°C. with palladised charcoal , though the same treatment removes a free -COOH group.

Experiment XIV, p.46. Preparation of carbazole-1-carboxylic acid. Carbazole-1-carboxylic acid was first prepared by the action of carbon dioxide on potassium carbazole at 270°C. In order to prove that tha acid prepared thus was actually the 1-carboxylic acid, Briscoe and Plant (J.1928,1990) oxidised tetrahydrocarbazole-8-carboxylic acid by refluxing for 12 hours with sulphur in quinoline. The acid so obtained required considerable purification, involving formation of the methyl ester, and hydrolysis again to the free carbazole-1-carboxylic acid. No yield is quoted. Moggridge and Plant (J.1937, 1125) dehydrogenated the methyl ester of tetrahydrocarbazole--8-carboxylic acid in quantitative yield with palladised charcoal in an atmosphere of hydrogen at 300-320°C for 14 hours. Tetrahydrocarbazole-8-carboxylic acid itself on this treatment gave carbazole. The ethyl ester of tetrahydrocarbazole-8-carboxylic acid has now been dehydrogenated in 75% yield by chloranil in boiling xylene, and the free acid readily obtained in 100% yield by hydrolysis.

Experiment XV, p.49. Preparation of 1-nitrocarbazole.

1-Nitrocarbazole can be prepared by the chromatographic separation of the products obtained by the direct nitration of carbazole, but the yield is small (Ziersch,Ber.1909, 42, 3797 ; Morgan and Mitchell, J.1931, 3283 ; Tucker and Co-workers, J. 1942, 500). Tucker and co-workers (J.1942, 500)

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also obtained an 18% yield of 1-nitrocarbazole by conversion of 7-nitro-1-phenyl-1:2:3:benztriazole by the Graebe-Ullmann method, and a 38% yield of the compound by decarboxylation with quinoline and copper bronze of 1-nitro-carbazole-3:6-dicarboxylic acid in a synthesis from 3:6-bistrichloroacetyl-carbazole.

This very important carbazole derivative has now been obtained by dehydrogenation of 8-nitro-1:2:3:4-tetrahydrocarbazole with chloranil in boiling xylene (6½ hour reflux) in 50% yield. As has been shown by later experiments, this yield would almost certainly be increased considerably by allowing a longer period of reflux.

Experiment XVI, p.51. Preparation of 3-nitrocarbazole.

Although there is already a very satisfactory method for the preparation of 3-nitro-carbazole by direct nitration of carbazole (Ziersch, Ber.1909,42, 3797), the method of obtaining it by chloranil dehydrogenation of 6-nitro-1:2:3:4-tetra-hydrocarbazole affords a useful alternative since it is synthetic and therefore independent of carbazole. Perkin and Plant tried to dehydrogenate the tetrahydrocompound by sulphur in quinoline but obtained a black resin. By chloranil dehydrogenation an 85% yield of 3-nitrocarbazole has now been obtained. (24 hour reflux).

Experiment XVII, p.52. Preparation of 2- and 4-nitrocarbazoles. 2- and 4-Nitrocarbazoles have not previously been prepared, although the corresponding tetrahydrocarbazoles have been investigated. Perkin and Plant (J.1921, 119, 1825) claimed that the compound (m.p.154°C.), obtained by cyclisation of cyclohexanone m-nitrophenylhydrazone was 7-nitro-1:2:3:4-tetrahydrocarbazole. Later, Collar and Plant (J.1926, 808) stressed the fact that only one isomer is obtained by cyclisation of cyclohexanone m-nitrophenylhydrazone, in contrast to the two acids they obtained by cyclisation of cyclohexanone m-carboxyphenylhydrazone . More recently, Plant (J. 1936, 899) reported that actually a mixture (m.p.151-152°C.) of 5- and 7-nitrotetrahydrocarbazoles is formed from cyclohexanone m-nitrophenylhydrazone, as is to be expected . He claimed that a 2:1 ratio of 5- and 7-isomers was formed, although the experimental section of his paper does not show clearly how he arrived at this 2:1 ratio. The 7-nitrotetrahydrocarbazole was identified by a reduction method, but Plant never isolated 5-nitrotetrahydrocarbazole.

It has now been proved that when cyclohexanone m-nitrophenylhydrazone is cyclised a molecular compound is formed, m.p. 154-155°C. This molecular compound was found to be readily broken up into the two isomers, in 1:1 ratio — 7-nitro-1:2:3:4-tetrahydrocarbazole m.p.171-2°C., and 5-nitro-1:2:3:4-tetrahydrocarbazole /

tetrahydrocarbazole m.p.155-156°C. This latter isomer was confirmed by mixed m.p. with the original molecular compound, and by analysis. Each of the isomeric tetrahydrocarbazoles readily provides a good yield of the corresponding nitrocarbazole by chloranil dehydrogenation, thus completing the series of mono-nitrocarbazoles.

Experiment XVIII, p.57. Alternative preparation of 2-nitrocarbazole. It was hoped that 7-nitrohexahydrocarbazole, readily prepared by nitration of hexahydrocarbazole with potassium nitrate in concentrated sulphuric acid, would yield 2-nitrocarbazole after a much shorter period of reflux with chloranil (cf. expt. X (b)). However it was found that the longer reflux required for nitrotetrahydrocarbazoles was also necessary here.

Experiment XIX, p.59. Alternative preparation of 2- and 4- nitrocarbazoles. 2- and 4-Nitrocarbazoles were prepared by reversing the order of procedure adopted in experiment XVII. That is, the 'molecular compound' was first dehydrogenated with chloranil in good yield, and then the product was chromatographed, yielding 2- and 4-nitrocarbazoles in approximately 1:1 ratio.

Analysis Figures of Nitrocarbazoles.

Compound	Experiment XVII			Experiment XVIII		Experiment XIX	
	C	H	N	C	H	C	H
2-nitro carbazole	(1) 66.7	3.79	13.1	66.1	3.53	66.0	4.16
	(2) 67.0	4.16				66.1	3.53*
4-nitro carbazole.	(1) 66.7	3.71	12.9			67.4	4.13
	(2) 67.4	4.12					

The theoretical figures are :-

C = 67.9% ; H = 3.8% ; N = 13.2% .

The first analyses of 2- and 4- nitrocarbazoles obtained in expt. XVII resulted in unsatisfactory figures for carbon, although the figures for hydrogen and nitrogen are excellent . Repetition after further crystallisation did not improve the analyses to any considerable extent. In fact , all the figures found for 2-nitrocarbazole are unsatisfactory although m.p.'s of the various samples obtained by different procedures were quite sharp, and gave no depression with each other. In only one case was a residue found*(analysis of 2-nitrocarbazole obtained by chromatographing following dehydrogenation).
It is quite impossible at this stage to say whether the unsatisfactory analyses are due to remaining impurities or whether these compounds require extra careful combustion treatment, and further investigation (including analyses of nitrocarbazoles obtained by other methods) is to be carried out before a decision can be reached.

SUMMARY.

(1). The application of the method of chloranil dehydrogenation to substituted tetrahydrocarbazoles, as well as to dihydrocarbazole, hexahydrocarbazole, and to a substituted hexahydrocarbazole, has been worked out, and has led to the successful preparation of many examples of various types of substituted carbazoles. The list of carbazole derivatives so prepared includes several important compounds which have never before been obtained, and all the mono-bromo and mono-nitrocarbazoles are now listed.

(2). Borsche had already proved the wide scope of the application of the Fischer indole synthesis to the preparation of substituted tetrahydrocarbazoles, but no dehydrogenation agent could be found suitable for all cases, i.e. a reagent which had no effect on all the possible substituent groups, e.g. halogen-, nitro-, carboxy-, etc.,etc. In the course of this research, the suitability of chloranil dehydrogenations in all cases has been proved, and during the discussion of experimental results, the superiority of chloranil over other dehydrogenation agents has been pointed out. The one disadvantage of this reagent - long period of reflux generally required - is certainly outweighed by its wide applicability and by the good yields of products so obtained.

(3) During the investigations on the use of this dehydrogenation /

dehydrogenation reagent, improved methods of preparation of the intermediate stages in the substituted tetrahydrocarbazole synthesis were introduced, and especially in the preparation of the substituted phenylhydrazines necessary for the syntheses.

All these improvements add to the efficiency of this highly satisfactory method of obtaining carbazole derivatives - by chloranil dehydrogenation of substituted tetrahydrocarbazoles.

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POSTSCRIPT.

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